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# THE SOCIAL AND ECONOMIC FACTORS AFFECTING THE INCIDENCE OF PREMATURE BIRTH

## Part I—Premature Births Without Complications of Pregnancy

BY

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### INTRODUCTION

IN his Annual Report for 1954, the Chief Medical Officer to the Ministry of Health expressed the opinion that "prematurity is the outstanding subject requiring investigation in the maternal and child welfare field". In this year 45,118 premature infants were born in England and Wales, which is nearly 7 per cent of all notified live births. Of these, 3,773 died within the first 24 hours and a further 3,323 died before the end of the fourth week. In addition more than 50 per cent of all notified stillbirths were premature. Twenty-eight per cent of premature births (as defined by birth weight) result in the loss of the infant either by still birth or death in the first four weeks.

About 50 per cent of premature births have no known cause and, of those with a recognized aetiology, 70 to 80 per cent are related to maternal toxaemia, congenital malformation and placenta praevia, whose causes again are largely unknown (Joint Committee of R.C.O.G. and B.P.A., 1949).

Various authors have noted the relationship between prematurity and adverse social conditions. For instance, in the United States, Eastman (1947) found that the incidence of premature births in a large maternity hospital was greater amongst white ward patients than private patients, and even greater among negro ward patients. Bakwin and Bakwin (1934) noted that newborn infants from a poverty stricken environment were smaller in all dimensions than those from a good environment. Bundesen (1951), in Chicago, reported on the incidence of premature birth in five socio-economic classes, classified according to the area in which the mothers lived, and found a percentage of 9·68 of all live births in the poorest area compared with 7·31 in the best area. In each area the incidence of premature births was higher amongst negroes. The most prosperous mothers were not included in this survey. Similarly, in Birmingham, Gibson and McKeown (1951) used the standard of housing as an indication of the economic circumstances of the parents and found that birth weight was slightly, but significantly, lower in the poorest group. This difference was not accounted for by differences in birth rank and was greatest when first births were compared.

In Scotland, Baird and Illsley (1953) have compared the incidence of prematurity in a group of mothers belonging predominantly to social classes III, IV and V, delivered of live-born infants in a maternity hospital, with those delivered in a private nursing home, who were mainly from social classes I and II. In the hospital group the incidence of prematurity was 7·6 per cent and in the nursing home group 4·8 per cent. The birth weight distribution within the two premature groups also differed widely, 12 per cent of the hospital premature infants being 4 pounds or less at birth compared with 6 per cent of the nursing home premature infants. The number of deaths before discharge was 6 times as high in the hospital group, although the mothers in this group received

specialist attention, and facilities for the care of the premature infants were excellent.

Numerous authors have commented on the relationship of social class to the neonatal and stillbirth rates (Baird, 1945; Woolf, 1947; Sutherland, 1949; Heady *et al.*, 1955; Morris and Heady, 1955a, b). Wastage from all causes is lower in social classes I and II, the most striking differences being in the categories of prematurity and unexplained intra-uterine death. In an analysis of all premature births occurring in Edinburgh Drillien (1956) found that the incidence of premature birth for primiparae in middle-class homes was 5·0 per cent compared with 10·3 per cent amongst the wives of semi-skilled and unskilled workers, while the percentage of babies over 7½ pounds at birth was 74 per cent in social class I compared with 36 per cent in social class V. When considering multiparae it was found that in the poorer homes the prematurity rate rose steadily after the second birth amongst poorer mothers while middle-class mothers maintained their low prematurity rate with all births after the first.

A different opinion is expressed by Douglas (1950). After analysing the figures for premature births in a national enquiry held in March, 1946, he states that social class differences in the risk of premature delivery are present but are relatively unimportant. Unfortunately the social class groupings used in this enquiry cannot be compared with the usual classification of occupations issued by the General Register Office (1951). Douglas divides his mothers according to occupation of husband, into four groups.

(1) Professional and salaried, which includes all the Registrar General's Class I, teachers and salaried administrators from Class II and salaried clerks from Class III.

(2) Black coated workers, i.e., all non-manual wage earners from classes II and III.

(3) Agricultural workers.

(4) Manual workers, i.e., remaining persons in Classes III, IV and V, this including skilled tradesmen together with unskilled labourers.

The groups were selected in this way because it was considered that mothers in the same group made similar use of the maternity and health services and expended about the same amount on child-bearing. The implicit assumption here is that these factors have an important bearing on the prematurity rate. If in fact these factors are not related to prematurity, this grouping, in particular the distribution of those from the Registrar General's Class III in the three of the four groups used by Douglas, may well have masked the true effect of social class on the prematurity rate.

Different investigators studying the effect of social conditions on birth weight have found an association between prematurity and the following:

(1) Maternal stature.
(2) Maternal diet during pregnancy.
(3) Illegitimacy.
(4) Level of antenatal care.
(5) Employment during pregnancy.

### (1) Maternal Stature

Baird (1949) examined the height and general physical condition of mothers delivered in a nursing home with those delivered in hospital. He had previously (1947) commented on the higher prematurity rate in the hospital group. He found that the percentage of women of 5 feet and under was 5 in the nursing home group and 26 in the hospital group. Likewise in the nursing home group 63·0 per cent of women were over 5 feet 4 inches compared with 23·5 per cent in the hospital group.

When the hospital group was analyzed in detail it was found that on the whole the tall women were healthier. He suggests that many of the small women are small not so much because of heredity but because they have been stunted by poor feeding during growing years.

Douglas and Mogford (1953a) also noted the relationship between prematurity and small maternal stature, when studying the development of a group of premature infants closely paired for social and economic circumstances with a group of full-time babies. Although they concede that this might be due to poor nutrition in early life, they think that genetic factors are the more important, as differences in height between mothers of premature and mature infants were just as large amongst relatively well-to-do pairs as amongst those from the manual worker group.

Thomson (1951) quotes a series, also from Aberdeen, in which a small but highly significant correlation was found between height and birth weight, but he did not consider that height by itself accounted for much of the variability in birth weights.

### (2) Maternal Diet During Pregnancy

The effect on the birth weight of supplementing the mother's diet has been noted by Ebbs *et al.* (1942) in Canada and Cameron and Graham (1944) in Glasgow. In the Canadian series the incidence of prematurity was 8·0 per cent in a group on a poor diet, 2·2 per cent in a group whose diet was supplemented and 3 per cent in a group whose diet was considered to be satisfactory and was not supplemented. In the Glasgow series the diet of one group of mothers was supervised during the last three months of pregnancy. Here the prematurity rate was 6·2 per cent compared with 10·0 per cent in a control group. On the other hand, Sontag and Wines (1947) in the United States found only an insignificant correlation between the level of maternal nutrition and birth weight. Burke *et al.* (1943), working on a small series of about 200 hospital confinements, go so far as to say: "If the diet of the mother during pregnancy is poor to very poor, she will in all probability have a poor infant from the standpoint of physical condition. If the mother's diet during pregnancy is excellent to good, her infant will probably be in good or excellent physical condition." The average birth weight for those on a good or excellent diet was 8 pounds 8 ounces compared with 5 pounds 13 ounces for those on a poor diet. The opposite point of view is put forward by Thomson (1951) who states: "The nutritional level of the individual patient is a poor guide to the probable birth weight of her baby. A change in diet during pregnancy within reasonably safe and practical limits is unlikely to influence the weight of her baby at term by more than a few ounces, which has little clinical importance in labour."

The effect of gross undernourishment of the mother on birth weight has been noted in countries affected by war and famine. Dean (1950) found a fall in average birth weight of about 6 per cent in Wuppertal during the period 1945 to 1946 when the food situation was at its worst; the average gestation period was only slightly reduced. A similar fall in average birth weight was found in Norway during the period of the occupation (Bøe, 1951).

In Holland during the six month period before the liberation when the food problem was acute the prematurity rate in urban districts was not significantly increased, although the average birth weight fell (Smith, 1947). During the Indian famine of 1943 there was only a 5·5 per cent reduction in average birth weight of babies born in a Calcutta Hospital (Edwards, 1946). During the siege of Leningrad (1941 to 1942) the incidence of prematurity rose to 28·2 per cent, and during the most severe period in the first half of 1942 it reached the peak rate of 41·2 per cent, but here the mothers not only suffered extreme hunger but were also subjected to severe and unaccustomed physical exertion as well as incessant bombardment (Antonov, 1947). The comparatively small fall in birth weight, in conditions of gross malnutrition, is surprising if as other workers maintain diet during pregnancy is of such importance.

### (3) Illegitimacy

A significant excess in the prematurity rate amongst single girls was found in an analysis of births in Edinburgh (Drillien, 1956). The incidence of prematurity was 8·7 per cent in the illegitimate group compared with 6·4 per cent of legitimate births. The effect on birth weight of prenatal care of the unmarried mothers is discussed by Toverud (1933) using as his material cases admitted to a home in Oslo. The average birth weight amongst a group of girls admitted 2 months or more before confinement was compared with that of a group admitted 6 weeks or less, and another group admitted just before delivery. The average birth weights in the three groups were 3,587 g., 3,347 g. and 3,240 g., giving a difference between the first and third group of about ¾ pound. A similar finding was reported by Peller (1948) who noted a lower perinatal mortality in unmarried mothers who rested in a home for 1 to 4 weeks or longer before delivery. These findings may be due to the effects of rest, good nutrition and antenatal care, but it may be that the girl from a better

background avails herself of assistance at an earlier date.

### (4) Level of Antenatal Care

In the national investigation into the maternity services carried out in 1946 by the Royal College of Obstetricians and Gynaecologists, and the Population Investigation Committee (1948) it was found that mothers of premature infants make less use of available antenatal services than mothers of babies born at term (Douglas, 1950). This was not thought to be due to greater youth or poverty. Amongst working-class mothers the incidence of prematurity in primiparae was 5·8 per cent in those receiving adequate antenatal care and 10·5 per cent in those receiving inadequate care. In multiparae the corresponding figures were 3·5 per cent and 9·3 per cent. Martin (1954) also found that mothers receiving a minimum or no antenatal care had a higher incidence of prematurity.

### (5) Employment During Pregnancy

In the national survey of the maternity services already referred to, it was found that the incidence of premature births was abnormally high amongst primiparae doing paid work during the last months of pregnancy. Thirty-five per cent of working-class mothers with premature babies were working during the last 15 weeks before the expected date of confinement, compared with 18 per cent of the control group. It also appeared that lack of domestic help is associated with a high risk of prematurity. Amongst working-class women confined in hospital, who stated that they had received domestic help from relatives during the last three months of pregnancy, the prematurity rate was 7·5 per cent compared with 10·7 per cent in those who had had no help. Amongst those confined at home the comparable rates were 6·5 per cent and 8·9 per cent. A similar association between employment during pregnancy and the risk of prematurity was found by Stewart (1955) studying first births in Northamptonshire. The percentage incidence of prematurity according to social class and gainful employment during pregnancy was as follows:

| Social Class | Housewives | Employed Less than 28 Weeks | Employed 28 Weeks or Longer |
|---|---|---|---|
| I and II .. | 2·6 | 3·3 | 5·9 |
| III .. .. | 4·0 | 8·5 | 10·4 |
| IV and V .. | 7·8 | 10·4 | 13·7 |

However, when comparing two samples of first babies weighing less than 5½ pounds at birth, and between 6½ and 8½ pounds, where careful matching was carried out for social class of father, occupation, age and height of mother, and pre- or post-marital conception, Illsley, Billewicz and Thomson (1954) found no difference between the groups in respect of paid work during pregnancy, domestic responsibilities or level of antenatal care. Martin (1954) also found no association between risk of prematurity and employment during pregnancy, or between duration of employment, hours of work or conditions of work. It seems likely that within each social class those from a better background would also be more likely to stop work earlier in the pregnancy and avail themselves fully of antenatal services.

### Method of Investigation

In the following study an attempt is made to assess in detail the relative importance of the various social factors which appear to have a bearing on premature birth. It is based on cases delivered in two Edinburgh maternity hospitals during the period 1953 to 1955. During that period about 75 per cent of all births in Edinburgh took place in hospital. Every case of premature birth, stillbirth and neonatal death was investigated together with a random sample, approximately equal in size, of full-time infants who survived to be discharged from hospital. The mothers were interviewed in private either by myself, or by one trained social worker, and information was obtained as to the mother's social status in childhood, before and after marriage. Clinical data regarding this and previous pregnancies and deliveries were obtained from the obstetrical records. The following information was sought and obtained in nearly every case:

(1) Social status in childhood:
  (*a*) Occupation of the father.
  (*b*) Unemployment of the father.
  (*c*) Housing.
  (*d*) Birth rank and number in family.
(2) Before marriage:
  (*a*) School leaving age.
  (*b*) Employment of the mother before marriage.
(3) After marriage:
  (*a*) Occupation of the husband.
  (*b*) Husband's weekly wage.
  (*c*) Housing.
  (*d*) Size of family.
  (*e*) Paid employment during pregnancy.
  (*f*) Extent of domestic duties and whether any domestic help was available during pregnancy.
(4) Data obtained from obstetrical records:
  (1) Attendances at antenatal clinic.
  (2) Height and weight.
  (3) Complications of this and previous pregnancies and deliveries.
(5) Diet:
  A proportion of women attending regularly for antenatal care in one hospital were interviewed by the hospital dietician, and an assessment made of their customary diet.

The social class classification used is based on that given in the *Classification of Occupations*, 1950 as follows:

Class I Professional, etc., occupations:
  e.g. Doctors, professional engineers, accountants, commissioned officers, company secretaries.
Class II Intermediate occupations:
  e.g. Industrial managers, business proprietors, pharmacists, costing clerks.
Class III Skilled occupations:
  e.g. Joiners, electricians, plumbers.
Class IV Partly skilled occupations:
  e.g. Farm labourers, railway firemen, bus conductors.
Class V Unskilled:
  e.g. Labourers, porters.

The Registrar General's Index classifies occupation according to skill rather than financial reward and some slight modifications have therefore been made in individual cases where it seemed that the economic circumstances of the home justified a placing in some other class than the one named in the Index. For example; farmers, farm managers, bailiffs and smallholders are all classified under social class II in the index with other agricultural workers in Class IV. In several cases where the father's occupation was given as smallholder and where the home background was obviously a humble one, the grandfather has been placed in social class III rather than II. Again miners are classified according to the type of work done; coal cutting and power loading machine men, hewers and getters being classified under social class III, other workers below ground being classified as social class IV. Where the grandfather was a miner it was usually impossible to define the exact nature of his work and, in view of the depressed state of the coal industry in the years when these mothers were children, all grandfathers who were miners were classified as social class IV. Today wages in all grades of mining are in line with those of skilled occupations generally, and those cases in which the husband is a miner are now classified as social class III irrespective of the type of work done. In addition to the five social classes already given, an additional social class VI has been added to cover those cases in which the grandmother was primarily responsible for the upbringing of the family owing to death, desertion or divorce before the child reached the age of five, or where the grandfather did not work because of disability, long periods of unemployment, or prison sentences, also all cases where the mother herself was illegitimate. Similarly social class VI was used when classifying occupation of husband, when the mother in question was widowed, divorced, or separated from her husband. Thus an attempt has been made throughout to classify the mother's home background according to economic circumstances; Classes I and II including comfortable, middle-class homes, Class III good artisan homes with reasonable economic security and Classes IV, V and VI the poorer working-class homes lacking financial security because of unemployment or low wages. Classification of the social class of the woman's own husband

has been easier as the weekly wage is nearly always known as well as the type of employment.

A preliminary analysis was made when the survey was in progress and it appeared that the social class of the mother's father was more closely correlated with the incidence of prematurity than that of her husband. It was therefore decided to interview a group of grandmothers in their own homes, in order to obtain further information about the mother's childhood. A group of about 100 cases were seen by one social worker. During these interviews more detailed information was obtained about the economic circumstances of the home, particularly regarding periods of unemployment of the grandfather, and a subjective assessment made of the type of home in which the mother was brought up. Comparison of the information given by the mother herself with that obtained from the grandmother indicated that the mothers did in fact give an accurate account of their early life, except for details of unemployment of the grandfather.

Table I gives the total number of legitimate, single births studied by parity and the presence or absence of complications of the pregnancy. It will be noted that in the sample studied nearly one-half of the premature births have no known aetiology, and that of the rest the majority are associated with maternal toxaemia, ante-partum haemorrhage and congenital defects. This accords with the findings in a previous study of factors affecting birth weight (Drillien, 1947) in which 51 per cent of premature births in primiparae were not associated with any complication of pregnancy and of the rest 35 per cent were associated with toxaemia of pregnancy, and 8 per cent with ante-partum haemorrhage. It is possible that the effect of social factors may be different in those with and without complications of pregnancy and for this reason the groups have been analyzed separately.

This paper deals in the main with the results found in the group of unknown aetiology. Subsequent papers will deal with the relation of social factors to premature births associated with various complications of pregnancy, and also with twin and illegitimate births.

## Analysis of the Data

### *Social Class of Mother's Husband and Father*

Information was always sought and nearly always obtained about the occupation of the mother's husband and her father, and this was used to assign them to their appropriate social classes according to the criteria already described. Social class of husband would be closely related to the mother's economic and social background since marriage, while her father's social class would be an index of her environment during childhood and early adult life. It is therefore of great interest to enquire into the relative importance of father's and of husband's social class as factors related to the risk of producing a premature baby.

The mean social class ratings were worked out for the fathers and the husbands of women in various groups, and the results are set out in Table II. Each value is followed by its standard deviation. Among the primiparae, those producing premature babies had husbands with a

Table I
*Legitimate Single Births: Numbers Sampled*

| Complications | Premature Parity | | | | | Mature Parity | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 1–2 | 3–4 | 5+ | Total | 0 | 1–2 | 3–4 | 5+ | Total |
| None .. .. | 107 | 58 | 9 | 10 | 184 | 154 | 116 | 22 | 5 | 297 |
| Toxaemia .. .. | 66 | 25 | 8 | 2 | 101 | 63 | 38 | 6 | 3 | 110 |
| A.P.H. .. .. | 21 | 39 | 19 | 4 | 83 | 11 | 10 | 5 | 2 | 28 |
| Congenital defects | 14 | 16 | 1 | — | 31 | 5 | 3 | — | — | 8 |
| Others .. .. | 12 | 11 | 5 | 2 | 30 | 11 | 12 | 6 | 2 | 31 |
| Total .. .. | 220 | 149 | 42 | 18 | 429 | 244 | 179 | 39 | 12 | 474 |

TABLE II
*Mean Social Class Ratings of Mother's Husband and Father*

| | | Husband | Father | Difference |
|---|---|---|---|---|
| All first births: | Premature .. | 3·087±·062 | 3·779±·080 | |
| | Mature .. | 2·876±·067 | 3·265±·081 | |
| | Difference .. | ·211±·092 | ·514±·114 | ·303±·146 |
| | t .. | 2·31 | 4·52 | 2·08 |
| | P .. | ·021 | ·000006 | ·038 |
| All second and third births: | Premature .. | 3·202±·086 | 3·924±·112 | |
| | Mature .. | 2·817±·082 | 3·171±·094 | |
| | Difference .. | ·385±·118 | ·753±·146 | ·368±·188 |
| | t .. | 3·25 | 5·14 | 1·96 |
| | P .. | ·0011 | ·000000002 | ·05 |
| First births, without complications: | Premature .. | 3·121±·087 | 3·888±·109 | |
| | Mature .. | 2·805±·082 | 3·208±·100 | |
| | Difference .. | ·316±·120 | ·680±·148 | ·364±·190 |
| | t .. | 2·64 | 4·59 | 1·92 |
| | P .. | ·0083 | ·000004 | ·055 |
| Second and third births, without complications: | Premature .. | 3·089±·133 | 3·786±·154 | |
| | Mature .. | 2·793±·094 | 3·103±·112 | |
| | Difference .. | ·296±·163 | ·683±·191 | ·385±·251 |
| | t .. | 1·82 | 3·58 | 1·53 |
| | P .. | ·069 | ·00003 | ·13 |
| Without complications, combined test: | P .. | — | — | ·023 |

mean class rating of 3·087, while the husbands of mothers in the control group had a mean rating of 2·876, which is 0·211 of a grade higher in the social class scale. This difference is 2·31 times its standard deviation, corresponding to a probability of only about 0·021 that it could be a chance effect, so it must be reckoned statistically quite highly significant. The difference between the average ratings of the fathers of the women in the two groups is much higher at 0·514, and this figure with a t value of 4·52 is overwhelmingly significant. For each group the fathers were rather lower down the social scale than the husbands. This is in accordance with the findings of the 1950 Census that there has been a marked decline since 1931 in the proportion of men in semi-skilled and unskilled occupations especially among men under 40. The last column of the table shows how much the disparity between fathers of the two groups, namely 0·514, differs from the disparity between husbands, namely 0·211. The difference is 0·303, which is statistically significant. It appears from this that the social class of a woman's father has a much greater influence than the social class of her husband on her risk of producing a premature baby, at any rate at her first pregnancy.

The second section of the table shows that this is true also for second and third pregnancies. The differences, 0·385 for husbands and 0·753 for fathers, are rather higher than those for the primiparous women, though not significantly so on statistical test. The contrast between husbands and fathers, 0·368, is significant at the 5 per cent probability point. The lower part of the table shows a similar analysis, confined to births without any complications of pregnancy.

This does not provide any independent new evidence since it relates to cases already included in the larger groups, but it is given separately to demonstrate that the same phenomena are true of the cases without complications, with which this paper is specially concerned. The last column shows that the contrast between differences for fathers and for husbands is if anything rather greater than for the whole body of cases. Due to smaller numbers, neither of the contrasts is statistically quite significant when taken alone, but a combined test by the standard method (Fisher, 1946, Section 21·1) gives a probability of only 0·023 that the two results, taken together, could be due to chance fluctuations.

This rather crude analysis does not necessarily give a correct estimate of the relative importance of husband's and of father's social class as influencing the risk of prematurity. The social class of a woman's father and her husband will be quite highly correlated. Although there is a fair amount of marrying up or down, on the average girls from lower class homes will tend to marry lower class husbands, and vice versa. When comparing mothers from middle class homes with the wives of labourers, even if there were no direct effect at all of the husband's social class on the risk of prematurity, one would still expect to find a difference, because the women with poorer husbands would have had poorer fathers. Similarly any comparison according to social class of father would tend to be distorted by the concomitant differences in social class of husband. To disentangle these two effects, one must resort to the technique of correlation and regression analysis.

Four regression equations were worked out, one for each of the categories of mothers specified in Table II. In each case occurrence of a premature birth was scored as a "dummy variate", whose multiple regression was calculated on the social class of husband and social class of father, and the significance of each of the regression coefficients was tested in the usual way. Table III gives the various tests of significance. It is clear that the regression on father's social class is always indubitably highly significant, whereas the regression on husband's social class, though not significant, is always in the expected direction, so there may be a residual effect after the father's social class is taken into account. But this independent influence is too small to show up clearly in the sample of 708 cases used for the regression equations, and could be reliably detected only in a survey covering several thousands. Be that as it may, it is certain that the social class into which a woman marries has only a very minor influence on her chance of having a premature baby in comparison with the influence of the social class in which she was born and brought up. From Tables II and III it is clear that this holds as much for second and third as for first pregnancies, although the woman will have been living at the standard of her husband's social class for several years longer.

Instead of using the Registrar General's social classification, one might take the husband's weekly earnings as an index of a mother's standard of living. For the groups having no complication of pregnancy the average earnings of the fathers are shown in Table IV. At each parity the fathers of mature babies earn more, as would be expected from their superior average social class rating. The higher earnings of fathers of second and third babies are no doubt due to the fact that the men are then several

TABLE III

*Tests of Significance for Regression Equations on Social Class of Husband and Father*

| | Husband's Social Class | | Father's Social Class | |
|---|---|---|---|---|
| | t | P | t | P |
| All first births | 0·48 | 0·62 | 3·91 | 0·0001 |
| All second and third births | 1·81 | 0·07 | 4·39 | 0·00001 |
| First births without complications | 1·09 | 0·28 | 3·81 | 0·0001 |
| Second and third births without complications | 0·26 | 0·79 | 3·00 | 0·0027 |

TABLE IV
*Pregnancies Without Complications*
*Average Earnings of Husbands*

| | Premature | Mature | Difference |
|---|---|---|---|
| Para 0 .. | £7 14s. | £8 12s. | 18s. |
| Para 1–2 .. | £8 15s. | £9 9s. | 14s. |

years older. In each of the groups there is a very big spread in the individual earnings. This is especially so in the two mature groups, where the excess in the average is largely due to the presence of a relatively small number with quite large incomes.

It would be expected that the earning capacity of a woman's husband would be correlated with the social class of her father, and this is confirmed by analysis of the data. The question then arises, how far the husband's earnings are directly related to incidence of prematurity, and how far they are merely an index of the wife's social class during her girlhood? To answer this question, regression equations have been worked out as before, and the results are summarized in Table V. After allowance is made for father's

TABLE V
*Tests of Significance for Regression Equations on Husband's Earnings and Father's Social Class*

| | Husband's Earnings | | Father's Social Class | |
|---|---|---|---|---|
| | t | p | t | p |
| First births .. | +1·07 | 0·57 | 4·37 | ·000025 |
| Second and third births | −1·05 | 0·59 | 3·46 | ·0011 |

social class, the regression of incidence of prematurity on husband's earnings in the first-born group is in the expected direction, but far below statistical significance. In the parity 1 and 2 group, the regression is in the opposite direction, and again far from significant. This is the sort of chance variation that would be expected if there was no real effect at all. On the other hand, regressions on father's social class are highly significant as before, so it must be concluded that the relation between husband's earnings and liability to prematurity is too small to be detectable in over 400 cases when the father's social class is also taken into account.

Illsley (1953) has studied the extent of intermarriage between social classes in primiparae in Aberdeen and points out that within social class III, the girl born into a small family who live in good conditions, who gets more than the minimum of education and takes a clerical occupation, tends to be well grown and of good physical grade and to marry into a higher social class, whereas the girl born into the same social class without the same social advantages tends to be smaller, and of poorer physique and to marry into a lower social class. It would therefore seem probable that the small residual effect of husband's social class which has been noted is due to such factors as these. Some multiple regressions were calculated to see whether these findings hold good for the mothers included in this investigation. The heights of the women were found to be significantly correlated with the social class of their husbands, after the correlation with social class of father had been taken into account. In other words, those who marry up tend to be rather taller, and those who marry down rather shorter, than the average in their class, just as found by Illsley. The effect, however, though statistically highly significant, is not very important judged by numbers of women affected. An advantage of one inch in height gives a girl a less than one-in-ten chance of rising one class rating by marriage. Illsley proposed to use the husband's social class as the most appropriate measure of class influences, on the ground that it not only reflects the conditions at the time of pregnancy, but is an equally good index of upbringing. He did not apply this or any other index to the incidence of prematurity in his sample. The results given above of the analysis by social class of father and of husband show that his proposal is not well founded. Use of his suggested index would not only lead to a serious underestimation of the influence of social and economic factors, but would also slur over the predominant part played by the mother's conditions during her girlhood.

Figure 1 shows the relative social class composition of the fathers of women having mature and premature babies. The great excess of lower

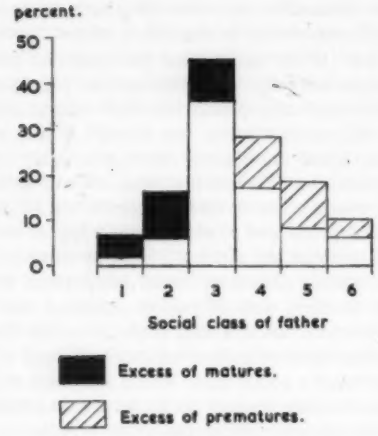


FIG. 1

Relative social class composition of fathers of women having premature and mature infants.

social class fathers in the premature group is very obvious. The relative risk of premature birth in relation to father's social class can be roughly estimated from Table VI. This gives the actual

TABLE VI

*Relative Risk of Premature Birth by Father's Social Class*

| Social Class | Premature | Mature | Premature/ Mature ×100 | Risk Relative to S.C. 3 |
|---|---|---|---|---|
| 1 and 2 | 26 | 91 | 29 | 44 |
| 3 | 112 | 174 | 64 | 100 |
| 4 | 87 | 101 | 86 | 134 |
| 5 and 6 | 87 | 57 | 152 | 237 |

numbers of fathers according to social class for the mature and premature groups, the two top and two bottom classes being combined to give adequate numbers. The next column is the number in the premature group expressed as a percentage of that in the mature group, and the last column shows these percentages multiplied by a factor so as to make the figure for social class III exactly one hundred. These values can be taken as the relative risks of giving birth to a premature baby, taking as standard the risk to daughters of skilled workers. This method of calculation exaggerates slightly the real contrast between the extremes, but the correction required would be quite small. It would be fair to say that the risk of having a premature baby for the daughters of well-to-do fathers is rather less than half that for daughters of skilled artisans; whilst the risk for daughters of unskilled fathers is rather more than double.

These findings give rise to an important question about the methodology of all enquiries into matters affecting infant and child mortality and welfare. The Registrar Generals of England and Wales and of Scotland publish extensive and valuable analyses according to social class of the child's father. They cannot of course take into account the social class of the child's maternal grandfather, since this is not stated on birth certificates, census forms, and other registration documents. But if the social class of the mother's father has anything like as close a relation to stillbirth and infant mortality rates as it has to risk of prematurity, it follows that comparison by social class of mother's husband will tend greatly to underestimate the true range of contrast attributable to social class differences. An indication that this may be so is given by Woolf (1947), who gives a diagram, his Figure 6, showing that the range between Class I and Class V for infant mortality in England and Wales is much less than the range between the best and the worst county borough, even though in the county boroughs babies of all social classes are lumped together. He suggests that this may be due to the residual effect of poverty in the past in certain areas. Similarly it may be seriously misleading to match premature babies with mature controls having fathers of like social class, and to assume that in this way social class differences can be allowed for, as was done, for example, by Douglas and Mogford (1953b). Table VII shows the average social class of mother's father for premature and for mature babies grouped according to social class of mother's husband. In each case the premature babies have mothers of considerably poorer origin. Now if a premature baby having, say a Class III father, was matched with a mature baby with a father of like class, the control baby would have a grandfather averaging about 0·4 of a social class higher. To put it another way, the premature baby would have a 60 per cent chance and the control baby only a 37 per cent

TABLE VII
*Average Social Class of Father According to Social Class of Husband*

| Social Class of Husband | Social Class of Father | |
|---|---|---|
| | Premature | Mature |
| 1 .. .. | 2·07 | 1·86 |
| 2 .. .. | 3·33 | 2·68 |
| 3 .. .. | 3·93 | 3·53 |
| 4 .. .. | 4·04 | 3·82 |
| 5 and 6 .. | 4·24 | 3·62 |

chance of having a mother brought up in Class IV, V or VI. It is of course possible and indeed likely that for some things studied, such as rate of development of physique and intelligence, the child's own home conditions, and hence the social class the mother married into, might have a greater relative influence. Nevertheless it is probable that in the management of her family the mother will be influenced by the environment of her own home and upbringing. From Tables III and V it would appear that, so far as liability to produce a premature baby is concerned, the husband's social class is if anything a more relevant measure than the husband's actual earnings. This is confirmed by Table VIII, which gives the first-order correlation coefficients between incidence of prematurity and the variables already considered.

TABLE VIII
*Coefficients of Correlation Between Risk of Prematurity and Various Criteria*

| | Para 0 | Para 1–2 |
|---|---|---|
| Husband's pay .. .. | 0·111 | 0·075 |
| Husband's social class .. | 0·158 | 0·137 |
| Father's social class .. | 0·270 | 0·261 |
| Mother's height .. .. | 0·170 | 0·156 |

The precise values depend on the composition of the sample, and the two columns are not strictly comparable. But comparison of the figures in the same column is legitimate. It will be seen that, although the husband's social class is much less relevant than social class of father, it is in each case a more relevant criterion than husband's earnings. It would seem therefore that, when father's social class is not recorded, the Registrar General's practice of using social class of husband is the best substitute. However Table VIII shows that, so far as prematurity is concerned, the mother's height seems to be a rather better index. It might be supposed that the actual wage, which is a precise figure, would give a better index than the social class, which includes a wide variety of occupations. The fact that this is not so indicates that the amount of money coming into the household is of less importance than the total cultural background which is shown rather better by the social class grading. This has been noticed also in a follow-up investigation which is in progress at present. Here it has been found that the standard of living in the home, as evidenced by the care and the upbringing of the family, is dependent on the cultural background of the parents rather than on the husband's pay packet. For example, in mining areas, where wages are at present above the average for working class families, the standard of child care tends to be lower than in some other homes where there is less money available. Many of the miners' wives are also daughters of miners, and will have been used, during their own early life, to the low standards consequent on the depressed state of the mining industry in the years before the war. In many cases the standard of living to which the mother was accustomed in her childhood, becomes the pattern for her own home after marriage.

Social class differences are an index of differences in nutrition, housing conditions, cultural background, and other such environmental factors. A discussion of the results will be deferred until some of these have been considered. Meanwhile, in analyses involving social class, the social class of mother's father will, as a rule, be used and the term "social class" is to be understood as referring to the mother's father unless otherwise stated.

*Birth Weight and Gestation Period*

The definition of a premature infant as laid down by the World Health Organization in 1948, which was generally accepted, but which is now held in question by certain obstetricians, runs as follows:

> "An immature infant is a live born infant with a birth weight of 5½ pounds (2,500 g.) or less. If weight is not specified a period of

gestation of less than 37 weeks may be considered as the equivalent of immaturity."

That the definition of prematurity based on weight alone is unsatisfactory is demonstrated in the national survey on *Maternity in Great Britain*, where 29 per cent of babies weighing 5½ pounds or less at birth were not considered premature by length of gestation (Douglas, 1950).

The advantage of using a weight basis in the definition of premature birth is obvious as this figure is measurable and less open to error. However, it appeared during the course of this study that quite a high proportion of babies, premature by weight, came within the normal limits of gestation, especially in those cases where the mother herself was small, and this has been investigated.

The period of gestation has been calculated to the nearest week, i.e., 38 to 39 weeks covers the period 37 weeks 4 days to 39 weeks 3 days.

Babies born before 38-weeks gestation have been considered premature, and those born 42 weeks or later, postmature.

Figure 2 shows the distribution of birth weights and of reported gestation periods in the premature groups of parity 0 and of 1–2 without complications of pregnancy, and Table IX gives the two-way classification of birth weight against gestation period. The birth weights show the expected steady increase up to 5½ pounds. The proportion weighing 5 to 5½ pounds is 46 per cent in the first-born group, considerably higher than the 37 per cent in the babies of parity 1–2. This fits in with the distribution of gestation times. The shaded areas and the entries to the right of the double lines in Table IX denote babies whose gestation time was given as 38 weeks or more, and who may therefore be considered full-term. In the primiparous group these amount to no fewer than 49 out of 99, or about 49 per cent, while in the higher parity group there are 19 out of 52, or 37 per cent.

It is of course rarely possible to determine gestation time with complete accuracy, and it is necessary to enquire whether this high proportion of apparently full-term babies can be an artefact due to misreporting by the mother. Table IX shows that there is a very close relation

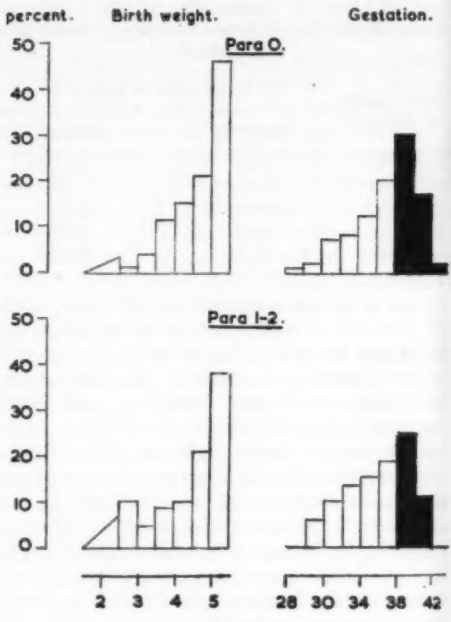


FIG. 2

Distribution of birth weight and reputed gestation time in premature births without complications of pregnancy.

between increasing gestation time and birth weight, and in fact the correlation coefficients are 0·662 for the firstborn group and 0·679 for the parity 1–2 group, so the relative precision of the reported gestation times must be quite high. It is of course possible that all the mothers systematically over-estimate their period of pregnancy, but it is difficult to see why they should do this, and there is some evidence to the contrary. Table X gives the correlation between height of mother and birth weight of baby in the two premature and the corresponding mature groups. Among the mature controls there is the expected positive correlation. But in the premature groups the relationship is reversed and the taller mothers tend, on the average, to have the smaller babies. This is what would be expected if the babies classed as premature because of low weight were a mixture of two categories:

TABLE IX
*Birth Weight and Length of Gestation for Premature Infants*

| | Pounds | Ounces | Gestation Period in Weeks | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | -28 | 28- | 30- | 32- | 34- | 36- | 38- | 40- | 42- |
| Para 0: | | | | | | | | | | | |
| Birth Weight | Less than 2 | 9 | 1 | — | 1 | — | — | — | — | — | — |
| | 2 | 9 | — | — | — | 1 | — | — | — | — | — |
| | 3 | 1 | — | 1 | 2 | — | — | 1 | — | — | — |
| | 3 | 9 | — | — | 1 | 4 | 1 | 1 | 3 | — | — |
| | 4 | 1 | — | 1 | 2 | 1 | 2 | 2 | 5 | — | 1 |
| | 4 | 9 | — | — | 2 | 1 | 4 | 6 | 5 | 2 | — |
| | 5 | 1 to 5 | 8 | — | — | — | — | 5 | 10 | 17 | 15 | 1 |
| Para 1–2: | | | | | | | | | | | |
| Birth Weight | Less than 2 | 9 | — | 1 | 1 | 1 | — | — | — | — | — |
| | 2 | 9 | — | 2 | 1 | — | 1 | — | — | — | — |
| | 3 | 1 | — | — | 1 | 2 | — | — | — | — | — |
| | 3 | 9 | — | — | — | 1 | — | — | — | — | — |
| | 4 | 1 | — | — | 2 | 1 | 1 | 1 | — | — | — |
| | 4 | 9 | — | — | — | 2 | 3 | — | 5 | 3 | — |
| | 5 | 1 to 5 | 8 | — | — | — | — | 3 | 9 | 8 | 3 | — |

(*a*) Babies who were small primarily because of premature delivery.

(*b*) Babies delivered at full-term, who were small because of the smallness of their mothers for reasons of genetic constitution or early malnutrition.

TABLE X
*Correlation Between Mother's Height and Birth Weight of Baby in Pregnancies Without Complications*

| | Mature | Premature |
|---|---|---|
| Para 0 .. .. | 0·1251 | −0·6240 |
| Para 1–2 .. .. | 0·2963 | −0·2932 |

If this were a true explanation, one would expect that the mothers of premature babies with full-term pregnancies would be smaller than those with shorter gestation periods, and Table XI shows that this is what is observed. Table IX confirms the expectation that the babies who are "premature by weight but mature by gestation" are mostly over 5 pounds, and nearly all over 4½ pounds, in birth weight. In the group of 5 to 5½ pounds well over half are reputedly of full-term gestation. It is of interest to note that the control groups of babies over 5½ pounds contain a few just over the borderline who are reported as being premature by gestation.

There is probably some misreporting, and some of the babies classified as "mature by gestation" may really be premature, and vice versa. But taken as a whole, the two groups, under 38-weeks gestation, and 38-weeks or more gestation, show contrasts like those set out in Table XI and recognition that there are two such groups helps to resolve apparent paradoxes in the analysis. The recognition of these two groups should be of value in the follow-up study, since it should make it possible to disentangle the consequences of premature delivery and of mere smallness at birth.

TABLE XI
*Average Height of Mothers of Premature Babies in Pregnancies Without Complications*

| | Height in Inches | | |
|---|---|---|---|
| | Under 38-weeks Gestation | 38-weeks Gestation and Over | All |
| Para 0 .. .. | 63·04 | 62·26 | 62·66 |
| Para 1–2 .. | 63·97 | 61·21 | 62·96 |

*Maternal Stature*

The mother's height has already been brought into consideration several times in the course of the foregoing analysis, and the following facts have been established.

(1) The mothers of premature babies are, on the average, significantly shorter than the mothers of the mature controls, and the correlation between stature and risk of prematurity is substantial.

(2) The average heights of the women increase as one goes up the social scale, whether the criterion is social class of father or social class of husband.

It might therefore seem logical to compute a multiple regression, just as was done for husband's social class and husband's earnings, to see whether the correlation between prematurity and mother's height can be wholly accounted for by the social class effect, or whether mother's height has some independent influence when social class has been allowed for. When this is done, it appears that, while the correlation of prematurity with stature is markedly reduced, there is still a partial regression which is on the verge of statistical significance.

However, some further facts have been established which suggest that this may not be the whole story. It has been shown:

(1) That whereas in the mature control group the heavier babies tend to be born to the taller mothers, in the premature group the opposite relation holds.

(2) The mothers, whose babies though full-term are "premature" on a weight basis, are on the average considerably shorter than those whose babies are genuinely premature by gestation time.

It therefore seemed desirable to divide the premature group into two, one labelled "Early", consisting of those with gestation period less than 38 weeks, and one labelled "Small", of gestation period 38 weeks or more, and to compare each of these groups separately with the mature controls consisting of babies over 5½ pounds at birth. Taking only births without complications of pregnancy, this gave four comparisons—Early against Mature for para 0 and for para 1 and 2, and Small against Mature for each of the two parity groups.

The first order correlation coefficients in each of these four aggregations are shown in Table XII. The coefficients are strictly comparable within each aggregation, but only roughly so from one aggregation to another. It will be seen that for all parities the correlation between early delivery and social class is substantial whereas the correlation with mother's height is small, and indeed statistically quite insignificant. On the other hand, the correlation between full-term smallness and mother's height is of about the same magnitude as that between smallness and social class. In each aggregation there is the expected correlation between the social class and height of the mother.

Multiple regressions for each of the four comparisons were worked out, and the tests of significance are shown in Table XIII. When social class and mother's height are simultaneously taken into account, it appears that stature has no independent relation to early delivery, the two regression coefficients being much less than their standard errors. On the

TABLE XII

*First Order Correlation Coefficients Between Variates Entering into Comparisons of Early Against Mature, and Small Against Mature Babies*

| Groups Compared | Variates Correlated | Para 0 | Para 1–2 |
|---|---|---|---|
| Early and mature | Earliness and social class | ·280 | ·159 |
| | Earliness and mother's height | ·069 | ·029 |
| | Social class and mother's height | ·247 | ·411 |
| Small and mature | Smallness and social class | ·181 | ·297 |
| | Smallness and mother's height | ·209 | ·272 |
| | Social class and mother's height | ·264 | ·507 |

TABLE XIII

*Significance Tests of Partial Regressions of Earliness and Smallness on Social Class and Mother's Height*

| Independent Variate | Dependent Variates | | Para 0 | Para 1 and 2 | Combined Parities |
|---|---|---|---|---|---|
| Earliness .. .. | Social class | t | 3·946 | 1·938 | 4·297 |
| | | p | ·00008 | ·053 | ·00002 |
| | Mother's height | t | −·046 | −·475 | −·418 |
| | | p | ·96 | ·63 | ·68 |
| Smallness .. .. | Social class | t | 1·873 | 2·245 | 2·769 |
| | | p | ·061 | ·025 | ·0056 |
| | Mother's height | t | 2·415 | 1·717 | 3·055 |
| | | p | ·016 | ·086 | ·0022 |

other hand, social class of father gives a highly significant regression for para 0, and one on the verge of significance for para 1–2, where numbers are smaller. By contrast, smallness seems to be influenced to about equal extents by social class and by mother's stature. In each case one of the regression coefficients is statistically significant and the other nearly so. To put the matter beyond doubt, combined regressions were calculated from the pooled variances and covariances of the two parity groups. Since the variances and covariances show no significant heterogeneity by the appropriate tests, it is legitimate to do this. The results are set out in the last column of Table XIII. In each case the regression on social class is very highly significant, and the regression of smallness on mother's height is also very highly significant. But the regression of early delivery on mother's height is negative, having a value that could have arisen twice out of three times by random fluctuations.

The following conclusions seem to be justified:

(1) That liability to premature delivery depends on the social class a woman was brought up in, and not at all on her stature.

(2) That liability to produce a small baby at full-term delivery is greater for short than for tall women. But among women of any given height, those low in the social scale have a greater risk than those of higher social origin.

*Age and Parity of Mother*

Among first births with no complications of pregnancy the average ages of mothers were:

Premature births — 26·28 years
Mature births — 25·26 years

In the premature group there is a small excess of mothers under 20, being 11·2 per cent compared to 8·4 per cent, and of mothers over 35, being 10·3 per cent compared to 3·3 per cent. For second and third births the mean ages are very similar, 29·57 for prematures and 29·52 for controls. There is no suggestion of any correlation between age of mother and weight of baby in any of the four groups. There is a very small negative correlation in each case between social class rating and age of mother, which accords with the known fact that women low in the social class scale tend to marry and reproduce rather younger than the better-off women. This correlation is much the same in the premature and control groups. For most of the subsequent analyses, age of mother can be regarded as of negligible influence, or as equally affecting the premature and control group, and it will therefore be left out of account.

This is in keeping with the findings noted in a previous study of all premature births in Edinburgh in 1953 to 1954 (Drillien, 1956). Here the birth weight distribution was found to be similar over the age period 20 to 34 years, but in those under 20 years and over 35 years the prematurity rate was about twice as high. It was suggested that the greater number of premature births in the youngest age group might be associated with the high incidence of premarital conception.

In the higher parity groups there are not enough cases to make valid deductions as to the

effect of parity on birth weight and in addition the selection of cases will be biassed by the fact that women with two or three living children are unlikely to be admitted for hospital confinement, in the absence of some complicating factor.

However, in the study of Edinburgh births already referred to, it was found that the higher prematurity rate was associated with first births and the lowest with second births. After the second birth the prematurity rate rose steadily with parity in the lower social classes, but mothers from social classes I and II maintained their low prematurity rate with all births after the first.

*Employment During Pregnancy*

Information was obtained as to whether each mother was employed during pregnancy, and if so, at what stage during pregnancy she gave up her job. The observations and analyses are presented in Tables XIV and XV. The top part of each table refers to births without complications. Among the primiparae, 39 out of 107, or 36·4 per cent, of those who had premature babies were not employed, compared with 57

TABLE XIV
*Duration of Paid Employment During Pregnancy*

| | | Not Employed | Month of Pregnancy When Employment Terminated | | | | | | | | | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | |
| No complications: | | | | | | | | | | | | |
| Para 0 .. | Premature | 39 | 2 | 2 | 10 | 11 | 9 | 17 | 13 | 3 | 1 | 107 |
| | Mature | 57 | 2 | 4 | 22 | 14 | 12 | 28 | 11 | 4 | – | 154 |
| Para 1–2 .. | Premature | 48 | 1 | 1 | – | – | – | 5 | 1 | – | – | 56 |
| | Mature | 100 | 1 | 2 | 1 | 3 | 1 | 4 | 1 | 2 | 1 | 116 |
| All births: | | | | | | | | | | | | |
| Para 0 .. | Premature | 78 | 4 | 8 | 21 | 12 | 17 | 29 | 16 | 7 | 3 | 195 |
| | Mature | 85 | 5 | 7 | 27 | 18 | 22 | 41 | 15 | 6 | – | 226 |
| Para 1–2 .. | Premature | 99 | 1 | 3 | 1 | – | 2 | 9 | 3 | 1 | – | 119 |
| | Mature | 139 | 1 | 3 | 3 | 4 | 2 | 7 | 1 | 2 | 2 | 164 |

TABLE XV
*Duration of Paid Employment During Pregnancy*

| No Complications Employment | Para 0 | | | | Para 1–2 | | | |
|---|---|---|---|---|---|---|---|---|
| | Number | | Percentages | | Number | | Percentages | |
| | Premature | Mature | Premature | Mature | Premature | Mature | Premature | Mature |
| Not employed .. | 39 | 57 | 36·4 | 37·0 | 48 | 100 | 85·7 | 86·2 |
| Less than 6 months | 34 | 54 | 31·8 | 35·1 | 2 | 8 | 3·6 | 6·9 |
| 6 months or more | 34 | 43 | 31·8 | 27·9 | 6 | 8 | 10·7 | 6·9 |
| | 107 | 154 | 100·0 | 100·0 | 56 | 116 | 100·0 | 100·0 |
| **All Births** | Number | | Percentages | | Number | | Percentages | |
| | Premature | Mature | Premature | Mature | Premature | Mature | Premature | Mature |
| Not employed .. | 78 | 85 | 40·0 | 37·6 | 99 | 139 | 83·2 | 84·8 |
| Less than 6 months | 62 | 79 | 31·8 | 35·0 | 7 | 13 | 5·9 | 7·9 |
| 6 months or more | 55 | 62 | 28·2 | 27·4 | 13 | 12 | 10·9 | 7·3 |
| | 195 | 226 | 100·0 | 100·0 | 119 | 164 | 100·0 | 100·0 |

out of 154, or 37·0 per cent, of those producing mature babies. The correspondence is remarkably close. The figures for those who were employed have been analyzed in various ways, all of which lead to the same conclusion. A simple form of analysis, into those working less than 6 months and those who worked till later, is shown in the table. Here again the percentages for the two groups of mothers are very similar, and the divergences are statistically quite insignificant. Among the mothers having second or third babies only about 1 in 7 was employed at all, and the divergences are well within the limits of chance sampling fluctuations. There is no indication that incidence of prematurity was associated with the fact or the duration of employment during pregnancy.

Since these results are not in accord with the findings of the National Survey, or of Stewart referred to above, some further analyses were made. It could happen that although there was no evidence of an effect of employment in births without complications, it might show up if all births were considered. Such an analysis is summarized in the lower part of the tables, and again there is a very close agreement between percentages for the premature and the mature groups. The National Survey found a particularly high incidence of prematurity among mothers doing paid work during the last month of pregnancy. In the present investigation the numbers who went on working in the eighth and ninth months were very small, being 11 out of 314 in the combined premature groups, and 10 out of 390 in the combined mature groups. There is no indication that this is an appreciable factor in the causation of prematurity.

*Antenatal Care*

From each mother a history was obtained of the antenatal care she had received, and the information was assessed in two ways. First, the women were classified according to the week of pregnancy in which they first attended the antenatal clinic. And second, they were graded according to whether, taking into account length and regularity of attendance and other relevant details, the care they had received was adequate or inadequate, with an intermediate group for borderline cases. Tables XVI and XVII give the data and the analysis for date of first attendance, the top part of each table referring to births without complications and the lower part to all births. The raw figures in Table XVI do not suggest any great difference between the various premature groups and their mature controls, and this has been borne out by comparisons according to number of different criteria. Perhaps the most relevant of these is the proportion of mothers who start attending within 16 weeks of conception. The facts are set out in Table XVII and show that the proportion is about 6 out of 7, and is remarkably similar for all the groups compared. Another criterion would be the numbers who received no antenatal care at all. Among the no complications groups, only one such case was reported, a primiparous mother of a premature baby, and

TABLE XVI
*Attendance at Antenatal Clinic*

| | | Week of First Attendance | | | | | | | | | No Attendance | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Up to 8 | 9 to 12 | 13 to 16 | 17 to 20 | 21 to 24 | 25 to 28 | 29 to 32 | 33 to 36 | 37 or more | | |
| No complications: | | | | | | | | | | | | |
| Para 0: | Premature .. | 19 | 52 | 18 | 8 | 6 | 2 | – | 1 | – | 1 | 107 |
| | Mature .. | 38 | 70 | 21 | 14 | 5 | 3 | – | 1 | 1 | – | 153 |
| Para 1–2 | Premature .. | 10 | 25 | 12 | 5 | 2 | 1 | – | – | – | – | 55 |
| | Mature .. | 29 | 55 | 20 | 7 | 1 | 1 | 1 | 2 | – | – | 116 |
| All births: | | | | | | | | | | | | |
| Para 0: | Premature .. | 48 | 94 | 27 | 13 | 6 | 3 | – | 1 | – | 2 | 194 |
| | Mature .. | 66 | 103 | 28 | 17 | 5 | 4 | – | 1 | 1 | – | 225 |
| Para 1–2: | Premature .. | 24 | 52 | 23 | 9 | 5 | 3 | 1 | – | – | 2 | 119 |
| | Mature .. | 35 | 74 | 25 | 9 | 2 | 2 | 1 | 2 | – | – | 160 |

TABLE XVII
*Proportion of Mothers Attending Antenatal Clinic in First 16 Weeks of Pregnancy*

| | | Total | First Attendance Up to 16 Weeks | |
|---|---|---|---|---|
| | | | Number | Percentage |
| No complications: | | | | |
| Para 0: | Premature | 107 | 89 | 83·2 |
| | Mature | 153 | 129 | 84·3 |
| Para 1–2: | Premature | 55 | 47 | 85·5 |
| | Mature | 116 | 104 | 89·7 |
| All births: | | | | |
| Para 0: | Premature | 194 | 169 | 87·1 |
| | Mature | 225 | 197 | 87·6 |
| Para 1–2: | Premature | 119 | 99 | 83·2 |
| | Mature | 160 | 134 | 83·8 |

in the whole sample there were 4 cases, all of them associated with premature births. If this difference between the mothers of premature and of mature babies was real, it would not give lack of all antenatal care more than a very minor importance. But it may be an illusory difference, due to the obvious fact that the mothers in the premature group have shorter gestation periods. A woman who would put off going to the clinic until say the thirty-fourth week counts as having attended if her pregnancy ran the full course. But if her baby was born prematurely in the thirty-third week, she would count as never having attended. From Table XVI it appears that in the no complications groups, the women who put off attendance until the thirty-third week or beyond numbered 4 in the mature groups, compared with 2 in the premature groups. For all births the corresponding figures are 5 for prematures and 4 for matures. There is no reason to suppose there are any real differences.

Table XVIII gives figures for the adequacy or otherwise of antenatal care in the no complications groups. Well over 90 per cent in every group were judged to have had adequate care, and the differences are small and statistically not significant. Although the data in this study give no indication that inadequate antenatal care is of importance in the incidence of premature birth, either for those with complicated or uncomplicated pregnancies, it is possible that some effect would be shown if a sample from the total population were studied. Over 90 per cent of the women delivered in these two hospitals received adequate care and most of those who did not receive adequate care were admitted as emergencies without previous hospital booking. It is possible that inadequate antenatal care may be found more commonly amongst women who elect to have their babies at home. However, as about three-quarters of all confinements in the country take place in hospital, improvement in antenatal services could only have a very small effect in reducing the overall prematurity rate.

TABLE XVIII
*Proportion of Mothers Receiving Adequate Antenatal Care*

| | | Adequate | Dubious | Inadequate | Total | Percentage Adequate |
|---|---|---|---|---|---|---|
| Para 0: | Premature | 96 | 2 | 7 | 105 | 91·4 |
| | Mature | 147 | 0 | 5 | 152 | 96·7 |
| Para 1–2: | Premature | 51 | 2 | 2 | 55 | 92·7 |
| | Mature | 105 | 2 | 8 | 115 | 91·3 |

Analyses were made to test whether there were any differences in amount or adequacy of antenatal care according to social class. There was no indication of any such differences.

*Mother's Diet*

For some of the mothers, information was available as to the adequacy of her customary diet. In one of the hospitals included in this study, all booked cases were expected to attend at the dietetic department and give details of their diets. Not all these women actually did attend. But for 332 of the mothers an evaluation of the diet was supplied by the dietician. These include women of all parities, and births with or without complications of pregnancy, there being too few cases to permit of sub-division. All cases attended before the fourth month of pregnancy. The information obtained is set out in Table XIX. About 37 per cent of the women having Early babies and 26 per cent of those having Small babies were adjudged to be consuming an inadequate diet, compared with under 18 per cent in the control Mature group. The difference between each of the premature sub-groups and the mature group was tested by the $\chi^2$ method, and the results are shown in the last two columns of the table. The excess of inadequate diets in the Early group was very highly significant, but the excess in the Small group, though in the expected direction, cannot be regarded as definitely established on the evidence of the small number of cases available.

The frequency of inadequate diets is correlated with social class, and the multiple regression technique was used to disentangle the two effects. So far as earliness is concerned, Table XX shows that inadequate diet seems to have an independent action even after social class is allowed for. In any given social class, the woman with an inadequate diet would appear to have an extra risk of delivery before full term. But for small full-term babies, an independent effect of inadequate diet cannot be demonstrated. If it exists, it will almost certainly be much less than the influence of diet on risk of earliness. It should be remembered that the evaluation of the diet refers to the woman's customary diet before and in the early months of pregnancy, not to the dietary habits throughout pregnancy.

All women who were judged to be taking an inadequate diet received special instruction and supervision and it is therefore probable that their diet during the later months of pregnancy would have been considered adequate.

*Information Obtained from the Maternal Grandmothers*

When 500 mothers had been seen, a preliminary analysis of the data was carried out. From this it appeared that social class of the

TABLE XIX

*Adequacy of Mother's Customary Diet in Relation to Outcome of Pregnancy*

| | Adequate | Inadequate | Total | Percentage Inadequate | Difference from Mature Group | P |
|---|---|---|---|---|---|---|
| Early .. .. .. .. | 37 | 22 | 59 | 37·3 | 10·534 | 0·0012 |
| Small .. .. .. .. | 46 | 16 | 62 | 25·8 | 2·095 | 0·15 |
| Mature .. .. .. .. | 174 | 37 | 211 | 17·5 | | |

TABLE XX

*Tests of Significance of Regressions of Earliness and Smallness on Adequacy of Diet and Social Class*

| Comparison | Independent Variate | Dependent Variates | t | P |
|---|---|---|---|---|
| Early and Mature .. | Earliness .. .. | Diet .. .. .. | 2·786 | 0·0053 |
| | | Social class .. .. | 2·970 | 0·0030 |
| Small and Mature .. | Smallness .. .. | Diet .. .. .. | 1·070 | 0·28 |
| | | Social class .. .. | 4·240 | 0·00003 |

woman's father was more closely related to her chance of having a premature baby, than that of her husband. It was therefore decided to interview a sample of grandmothers in their own homes, in order to obtain more detailed information about the economic circumstances of the girl's early life. No grandmothers from social classes I and II were seen as it was assumed that mothers from these homes would have had a comfortable background. About one hundred grandmothers were interviewed. In each case the daughter was under thirty years of age and having her first, second or third baby. All interviews were carried out by one social worker.

The approach varied with the individual, but in most cases after a preliminary explanation the grandmothers talked freely. In some cases the visit was obviously resented, and the woman was not pressed to give information of a confidential nature. Information was obtained from each grandmother as to the occupation of her husband during her daughter's childhood, and this was found to tally very closely with what the mothers themselves said. They were also asked about wages and periods of unemployment. The most important information sought was an assessment of the grandmother's likely efficiency as a housewife and mother, as evidenced by the condition of her house, her personal appearance and the general impression obtained from conversation. This assessment was a purely subjective one, but it can be considered valid as all interviews were carried out by one person, who observed the same standards throughout. The grandmothers were rated as being superior, average or poor.

Table XXI gives the numbers and percentages of grandmothers of these grades, classified according to whether their daughters had a premature or a mature baby. There is clearly a very marked preponderance of superior grades in the mature group, and of average and poor grades in the premature group, and the appropriate statistical test shows that this is overwhelmingly significant. Grade of grandmother is however correlated with social class, and the multiple regression method was used to separate the two effects. The results are shown in Table XXII. The first order correlation between risk of prematurity and grade of grandmother is the highest of all those found between prematurity and any relevant factor. On the other hand, the correlation between prematurity and social class

TABLE XXI

*Efficiency Grade of Grandmother in Relation to Outcome of Pregnancy*

| | Numbers | | Percentages | |
|---|---|---|---|---|
| | Premature | Mature | Premature | Mature |
| Superior .. .. .. .. .. .. | 16 | 29 | 27 | 61 |
| Average .. .. .. .. .. .. | 25 | 13 | 42 | 28 |
| Poor .. .. .. .. .. .. | 18 | 5 | 31 | 11 |
| Total .. .. .. .. .. | 59 | 47 | 100 | 100 |

$\chi^2$ for trend = 12·96. P = 0·0003.

TABLE XXII

*Regression of Risk of Prematurity on Grade of Grandmother and Social Class*

| | | |
|---|---|---|
| First order correlation coefficients: | | |
| Prematurity and grade of grandmother .. .. .. .. .. | 0·350 | |
| Prematurity and social class .. .. .. .. .. .. | 0·232 | |
| Grade of grandmother and social class .. .. .. .. .. | 0·369 | |
| Partial regression coefficients: | | |
| Prematurity: | t | p |
| Grade of grandmother .. .. .. .. .. .. | 2·968 | ·003 |
| Social class .. .. .. .. .. .. .. .. | 1·194 | ·23 |

TABLE XXIII
*Unemployment of Grandfather in Relation to Outcome of Pregnancy*

| Unemployment of Grandfather | Numbers | | Percentages | |
|---|---|---|---|---|
| | Premature | Mature | Premature | Mature |
| Little or none .. .. .. .. .. | 23 | 27 | 39 | 57 |
| Intermittent .. .. .. .. .. | 14 | 8 | 24 | 17 |
| Chronic .. .. .. .. .. .. | 22 | 12 | 37 | 26 |
| | 59 | 47 | 100 | 100 |

$\chi^2$ for trend=3·104. P=0·078.

is rather lower than in the general body of data, no doubt because the sample of grandmothers did not extend to social classes I and II. Multiple regression of risk of prematurity on both variates showed that grade of grandmother gives a highly significant coefficient even when social class is allowed for, and that the figure for social class, though in the expected direction, is not statistically significant. On a selected sample of only 106 cases, this negative result need not be taken very seriously, but it can be regarded as established that a girl's type of upbringing, as judged by the apparent efficiency of her mother, has a very close bearing on her risk of producing a premature baby.

From information given by the grandmothers, their husbands were classified according to whether they had been seldom or never, intermittently, or chronically unemployed during the girlhood of the mother, and the results are shown in Table XXIII related to the outcome of the pregnancy. There is clear indication that risk of prematurity is associated with unemployment. The statistical test shows that this just falls short of significance, though the P value can be halved to ·039 since the trend is in the expected direction. Since degree of unemployment seems to be correlated both with social class and with efficiency of grandmother, it is possible that the independent influence of unemployment might be much diminished or neutralized if these were allowed for. But on the small sample available this did not seem worth pursuing. Analysis was also made of the relation between risk of prematurity and whether the grandmother had no, part-time, or full-time paid employment during the upbringing of the mother. This showed no difference between the premature and mature groups.

In 44 cases when a grandmother had been interviewed, it also happened that the mother had been assessed for adequacy of diet. An analysis of these cases is shown in Table XXIV.

TABLE XXIV
*Efficiency Grade of Grandmother in Relation to Adequacy of Mother's Customary Diet*

| Grade of Grandmother | Diet | | Total |
|---|---|---|---|
| | Adequate | Inadequate | |
| Superior .. | 17 | 2 | 19 |
| Average .. | 15 | 3 | 18 |
| Poor .. .. | 1 | 6 | 7 |
| | 33 | 11 | 44 |

$\chi^2$ for trend=11·50. P=·0007.

There is an obvious tendency for inadequate diet in the daughter to be associated with inefficiency in the mother, and, although the sample is small, this trend is statistically very highly significant. So it would appear that the way a woman feeds herself and her family after marriage is conditioned, at any rate in part, by the kind of diet she received as a child.

## DISCUSSION

A full discussion of the problem under review will be left until the data on complicated pregnancies and twin and illegitimate births have been analyzed. Meanwhile the following tentative conclusions seem justified. First it should be remembered that an investigation such as this

can throw light on the causes of the phenomenon studied only in so far as differences can be observed between groups, which can be classified according to some objective criterion such as social class. Nearly all the women studied in this sample had received adequate antenatal care, lived at a reasonably high standard of living, and had been educated up to the age of 14 years. Therefore it cannot be assumed from any negative conclusions that gross poverty during pregnancy might not have an effect on the birth weight of the baby. There may be no contradiction between these findings and those made in the past when differences between classes were greater.

In addition although the incidence of prematurity is low amongst women brought up in a good environment, yet a small number of cases do occur. For example, one woman whose father was a clergyman in a comfortable living, whose height was 5 feet 6 inches, and general health excellent, of good physique, married to a professional man and used to a high standard of living, produced a baby, her third, weighing 2 pounds 10 ounces at 31-weeks gestation. There was no complication of the pregnancy, and her 2 previous children, born 2 and 4 years previously, were full-time and weighed 6 pounds 10 ounces and 6 pounds 3 ounces respectively. This study throws no light on such cases as this. Nevertheless wide differences in the risk of producing a premature infant are shown between the highest and the lowest social classes, as demonstrated by the fact that amongst women from the poorest working class homes the risk of prematurity was four times as high as that amongst women from comfortable middle class homes. The following positive results appear well established; the social class of upbringing and the efficiency of the grandmother are the two most important factors related to the risk of prematurity. This appears to apply more or less equally to babies premature by weight and gestation and to small full-time infants. In other respects a distinction must be made between these two categories. So far as the early babies are concerned the other factor implicated is the mother's customary diet before pregnancy. It appears probable that the diet after marriage is related to the diet to which the girl was accustomed in her own home. If this is so, and an inadequate diet throughout childhood and early adult life increases the liability to having a premature infant, then by the time the woman becomes pregnant the damage is already done, and improvement of the diet during pregnancy would have little effect. So far as the small full-time babies are concerned the height of the mother is also of importance, but this is not the sole factor, social class having an equal effect. There is no doubt that the question of inheritance is relevant when considering the small full-time infant, but it seems probable that some of the short mothers are short not only for reasons of genetic constitution, but also as a result of early malnutrition.

In spite of the small residue of cases of premature birth where social factors do not appear to have any bearing, any attempt to produce a substantial reduction in the incidence of prematurity must concentrate on the next generation. Improved standards of child care and nutrition and improved education of potential mothers should lead to a fall in the type of premature birth, which in this study appears to be so highly correlated with poor social and economic conditions in the past.

## Summary

A statistical analysis is presented of a study into the social and economic factors affecting liability to premature birth. The sample consisted of all cases of premature birth, stillbirth and neonatal death occurring in two Edinburgh hospitals over a 2-year period, together with a control group, approximately equal in size, of mature babies. Over one thousand cases were investigated. The information was obtained by personal interview. This paper deals mainly with cases having no complication of pregnancy.

The following conclusions were reached:

(1) Using the technique of correlation and regression analysis it was found that the social class into which a woman marries (i.e., that of her husband) has only a very minor influence on her chance of having a premature baby compared with that in which she was born and brought up (i.e., that of her father). This applies for complicated and uncomplicated pregnancies,

and for women having their first, second and third babies.

(2) If the social class of the woman's father is not known, the social class of her husband is a more relevant criterion than husband's weekly wage.

(3) When gestation time was taken into account it was found that one-half of the premature infants born to primiparous women and one-third of those born to women in the higher parity group were reported as having a gestation time of 38 weeks or longer.

Whereas in the mature control group height of mother was positively correlated with weight of baby, in the premature group the relationship is reversed. It was concluded that babies classed as premature on a weight basis were a mixture of two categories, early and small. The mothers of small babies were significantly shorter than those with early babies.

(4) Where social class and mother's height were considered together it was found that:

(*a*) Liability to early delivery depends on the social class of upbringing and not at all on stature.

(*b*) Liability to produce a small baby is affected about equally by social class and maternal stature.

(5) No effect on the liability to premature birth could be demonstrated in women who held paid employment during pregnancy or who received inadequate antenatal care.

(6) In any given social class, the woman whose customary diet was considered inadequate appeared to have an extra risk of premature delivery. For small full-term babies no independent effect of inadequate diet could be demonstrated.

(7) The efficiency of the grandmother was highly correlated with liability to premature birth in the next generation. There was also an obvious tendency for inadequate diet of the woman to be associated with inefficiency of her own mother.

(8) An association was found between risk of prematurity and unemployment of the grandfather. No association was found between this risk and paid employment of the grandmother.

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## References

Antonov, A. N. (1947): *J. Pediat.*, **30**, 350.
Baird, D. (1945): *J. Obstet. Gynaec. Brit. Emp.*, **52**, 217.
Baird, D. (1947): *Lancet*, **2**, 531.
Baird, D. (1949): *Lancet*, **1**, 1079.
Baird, D., and Illsley, R. (1953): *Proc. R. Soc. Med.*, **46**, 53.
Bakwin, H., and Bakwin, R. (1934): *Human Biol.*, **6**, 612.
Bøe, F. (1951): *Acta obstet. gynec. scand.*, **30**, 247.
Bundesen, H. N. (1951): *Annual report of the Chicago Health Department.*
Burke, B. S., Beal, V. A., Kirkwood, S. B., and Stuart, H. C. (1943): *Amer. J. Obstet. Gynec.*, **46**, 38.
Cameron, C. S., and Graham, S. (1944): *Glasgow med. J.*, **142**, 1.
Dean, R. F. A. (1950): *Proc. R. Soc. Med.*, **43**, 273.
Douglas, J. W. B. (1950): *J. Obstet. Gynaec. Brit. Emp.*, **57**, 143.
Douglas, J. W. B., and Mogford, C. (1953a): *Arch. Dis. Childh.*, **28**, 436.
Douglas, J. W. B., and Mogford, C. (1953b): *Brit. med. J.*, **1**, 748.
Drillien, C. M. (1947): *J. Obstet. Gynaec. Brit. Emp.*, **54**, 300.
Drillien, C. M. (1956): *Arch. Dis. Childh.*, **31**, 390.
Dunham, E. C. (1955): *Premature infants.* 2nd ed. Cassell, London.
Eastman, N. I. (1947): *Amer. Pract.*, **1**, 343.
Ebbs, J. H., Brown, A., Tisdall, F. F., Moyle, W. J., and Bell, M. (1942): *Canad. med. Ass. J.*, **46**, 6.
Edwards, N. (1946): *J. Ass. med. Women, India*, **34**, 19.
Fisher, R. A. (1946): *Statistical methods for research workers.* 10th edition. Oliver and Boyd, Edinburgh.
General Register Office (1951): *Classification of occupations, 1950.* H.M. Stationery Office, London.
Gibson, J. R., and McKeown, T. (1951): *Brit. J. soc. Med.*, **5**, 259.
Heady, J. A., Stevens, C. F., Daly, C., and Morris, J. N. (1955): *Lancet*, **1**, 499.
Illsley, R. (1953): *Proc. R. Soc. Med.*, **46**, 53.

Illsley, R., Billewicz, W. Z., and Thomson, A. M. (1954): *Brit. J. prev. soc. Med.*, **8**, 153.
Martin, F. M. (1954): *Med. Offr.*, **92**, 263.
Morris, J. N., and Heady, J. A. (1955a): *Lancet*, **1**, 343.
Morris, J. N., and Heady, J. A. (1955b): *Lancet*, **1**, 554.
Peller, S. (1948): *Population Stud.*, **1**, 405.
Royal College of Obstetricians and Gynaecologists and Population Investigation Committee (1948): *Maternity in Great Britain*. Oxford University Press, London.
Smith, C. A. (1947): *J. Pediat.*, **30**, 229.
Sontag, L. W., and Wines, J. (1947): *Amer. J. Obstet. Gynec.*, **54**, 994.
Stewart, A. (1955): *Brit. J. prev. soc. Med.*, **9**, 159.
Sutherland, I. (1949): *Still births: their epidemiology and social significance*. Oxford University Press, London.
Thomson, A. M. (1951): *Brit. J. Nutr.*, **5**, 158.
Toverud, K. V. (1933): *Amer. J. Dis. Child.*, **46**, 954.
Woolf, B. (1947): *Brit. J. soc. Med.*, **1**, 73.

# OBSERVATIONS ON THE OXYGENATION OF THE FOETUS IN NORMAL AND ABNORMAL PREGNANCY

BY

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FOR many years it has been thought that certain changes in the placenta might be related to pregnancy toxaemia. Although it was considered by some that these infarcts, haemorrhages and the like might be implicated in the cause of pre-eclampsia, by most they were considered to be degenerative and consequent on the failure of an adequate maternal blood supply for chorionic nourishment. The original hypotheses based on placental disease have been modified from time to time as medical knowledge has advanced and the placental ischaemia theory still is regarded by many as a satisfying one. Many obstetricians are unable to accept any theory based on the suggestion that unknown substances are released from the diseased placenta and thus lead to the signs and symptoms of toxaemia. They are, however, prepared to accept the fact that consequent on the establishment of the toxaemic process the normal process of gradual placental senescence is accelerated and thus leads to serious defects in its function of nourishing the infant. That the infant born from a mother who has had toxaemia for some time is likely to be small has long been known. The fact that it does not readily survive more than the simpler hazards of birth has also been long a matter of acute clinical interest.

In a long term study of placental respiratory function it became necessary to determine not only the oxygen needs of chorionic tissue but to correlate this with its ability to transmit oxygen to the foetus. A survey of the literature on oxygen transfer from mother to foetus in the human being showed that although a certain amount was known about this since Eastman's pioneering studies in 1930, his own and subsequent studies were largely concerned with the effects of oxygen and anaesthesia on the foetal cord blood at birth and on the initiation of respiration. In fact, the only two important contributions to our knowledge of the oxygenation of the foetus in normal and abnormal pregnancies are those of Clemetson and Churchman (1953) and Walker and Turnbull (1953). The results obtained by these workers are not in agreement, particularly with regard to the findings obtained in babies born from pre-eclamptic mothers. Walker and Turnbull (1953) had taken the precaution of studying the cord oxygen levels at various periods of gestation and, as Barcroft, Kennedy and Mason (1940) had shown in the sheep, they showed that in the human the cord oxygen levels fell as pregnancy advanced to term and beyond. The discrepancy between the work of these two groups was such that we felt compelled to re-investigate the whole subject using perhaps a larger normal and abnormal group than had been employed before.

## METHODS

Immediately after delivery, and before the onset of respiration, the cord was occluded simultaneously at both ends to stop all circulation, two pairs of Spencer Wells forceps being applied at each end. Clamping of the cord has been shown by Minkowski *et al.* (1953) to cause no significant change in the oxygen levels. A variable length of cord, usually about 8–10 inches, was obtained by cutting between the forceps. The blood from the umbilical vein and arteries was immediately aspirated under liquid paraffin, transferred anaerobically to heparinized containers and analyzed at once.

Oxygen contents in volumes per cent were

estimated in duplicate in the constant volume manometric apparatus by the method of Van Slyke and Neill (1924), modified as described by Orcutt and Waters (1937). Samples of 0·5 ml. of blood were used for each determination.

Oxygen capacities were estimated in duplicate, also by the Van Slyke method, where sufficient blood was available. Most samples from the umbilical vein were sufficient for capacity determinations, about 5–10 ml. being available, but in almost half of the samples from the arteries only about 2–3 ml. were obtained.

Haemoglobin levels were also estimated in duplicate on both samples by the oxyhaemoglobin method described by Arnold (1949), using the Spekker photo-electric absorptiometer. Occasionally there was some slight discrepancy between the levels of haemoglobin in the vein and arteries, probably due to a degree of stasis caused by kinking of the vessels. This was confirmed by estimations of the oxygen capacity of both samples where possible, 1 g. of haemoglobin combining with 1·34 ml. oxygen.

Since oxygen capacities were not estimated in all the samples, the capacity of each sample was calculated from the haemoglobin level (oxygen capacity (vols. per cent)=haemoglobin (g./100 ml.)×1·34), actual determinations being used as a constant cross check of the results. The percentage oxygen saturation is given by (oxygen content÷oxygen capacity)×100.

## Material

In all, 240 cases were studied. The majority of samples were obtained after an uncomplicated spontaneous vertex delivery, where there was no evidence of cord obstruction and where chloroform was administered only with the birth of the head. This uniformity in method of delivery permitted comparison between the normal term, premature, postmature and pre-eclamptic groups. Although the results obtained may not give a true picture of the oxygen levels in the umbilical cord *in utero*, the conditions of the experiment were as nearly constant as possible and the results were not influenced by the increased number of variable factors associated with instrumental and operative deliveries. A series of the latter were also studied as well as a few twin pregnancies, breech deliveries and cases in which there was potential cord obstruction or undue delay during delivery.

The normal cases (112) had an uneventful pregnancy with a blood pressure recording of less than 130/80, no albuminuria, no more than a slight trace of ankle oedema, no excessive weight gain and no vaginal bleeding during pregnancy. All the infants survived. Excluded from this group were all cases in which (1) the cord was potentially obstructed (round the neck or limb at birth, or unduly short and under tension), (2) oxygen was administered during labour, (3) heavy sedation was administered within 2 hours of delivery, (4) there was undue delay or difficulty at delivery, or (5) there was doubt as to the duration of pregnancy. The duration of pregnancy was calculated to the nearest week from the first day of the last menstrual period and in the majority of cases studied this was fairly accurately known as the patients were booked cases who had attended the antenatal clinic from the early weeks of pregnancy.

Of the cases complicated by pre-eclampsia, 38 had a spontaneous vertex delivery with chloroform administered during the birth of the head in all but 3 of the very premature cases. Again all the infants survived. All cases of cord obstruction and delayed delivery were excluded and no patients received oxygen during labour, but 4 of the premature severe cases had fairly heavy sedation during labour: luminal, pethidine and heroin.

Not all were booked cases, 10 being admitted to hospital because of toxaemia, so the duration of the pregnancy and pre-eclampsia was not known for certain in all cases.

The cases of forceps delivery and Caesarean section following normal and abnormal pregnancy are recorded under a separate heading.

## Results

### Part I. Normal Pregnancy

Table I shows the average results obtained in the 112 cases of normal pregnancy mentioned above with reference to the duration of pregnancy in weeks. The individual results are recorded elsewhere (MacKay, 1955).

This study is concerned mainly with the levels of oxygen content and oxygen saturation in the

TABLE I

*Showing the Average Results in Normal Cases from the 35th to 43rd Week of Pregnancy*

| Duration of Pregnancy (Weeks) | No. of Cases | Umbilical Vein | | | Umbilical Arteries | | |
|---|---|---|---|---|---|---|---|
| | | Oxygen Content Volumes Per cent | Haemoglobin g./100 ml. | Oxygen Saturation Per cent | Oxygen Content Volumes Per cent | Haemoglobin g./100 ml. | Oxygen Saturation Per cent |
| 35 | 1 | 17·17 | 16·2 | 79·1 | 9·64 | 16·4 | 43·9 |
| 36 | 4 | 16·82 | 17·1 | 73·5 | 9·06 | 16·9 | 40·3 |
| 37 | 11 | 16·61 | 16·6 | 74·5 | 8·82 | 16·8 | 39·1 |
| 38 | 10 | 16·32 | 17·5 | 69·7 | 8·46 | 17·7 | 35·8 |
| 39 | 13 | 15·33 | 17·7 | 64·7 | 7·33 | 17·7 | 30·9 |
| 40 | 30 | 14·64 | 17·2 | 63·5 | 7·21 | 17·3 | 31·0 |
| 41 | 17 | 15·57 | 17·7 | 65·7 | 7·50 | 17·7 | 31·8 |
| 42 | 19 | 12·60 | 17·7 | 53·5 | 4·86 | 17·7 | 20·5 |
| 43 | 7 | 13·33 | 18·2 | 55·0 | 4·76 | 18·3 | 19·3 |

cord vessels as pregnancy proceeds to term and thereafter.

The average oxygen content (volumes per cent) of the blood in the umbilical vein shows a gradual fall from 17·17 vols. per cent in the single case at 35 weeks to 13·33 vols. per cent in the 7 cases at 43-weeks gestation, with a marked similarity of the results at 39 weeks (15·33 vols. per cent), 40 weeks (14·64 vols. per cent) and 41 weeks (15·57 vols. per cent). After the 41st week the drop in oxygen content is most marked (see Table I).

The average oxygen content (volumes per cent) in the umbilical arteries shows a parallel fall as pregnancy continues, from 9·64 vols. per cent at 35 weeks to 7·21 vols. per cent at 40 weeks, with a further drop to 4·76 vols. per cent at 43 weeks. The arteriovenous difference remained fairly constant at 7·5–8·5 vols. per cent throughout.

Throughout the series there was a fairly marked scatter with considerable overlapping from week to week.

The haemoglobin levels, and therefore the oxygen capacities, showed a very marked variation throughout although there appears to be a rise in the average results (see Table I) from the single case at 35 weeks (16·2 g./100 ml.) and the 11 cases at 37 weeks (16·6 g./100 ml.) to the 7 cases at 43 weeks (18·2 g./100 ml.).

Figure 1 shows the progressive fall in the average oxygen saturation of the cord blood as pregnancy matures to term and continues thereafter. In the umbilical vein the average

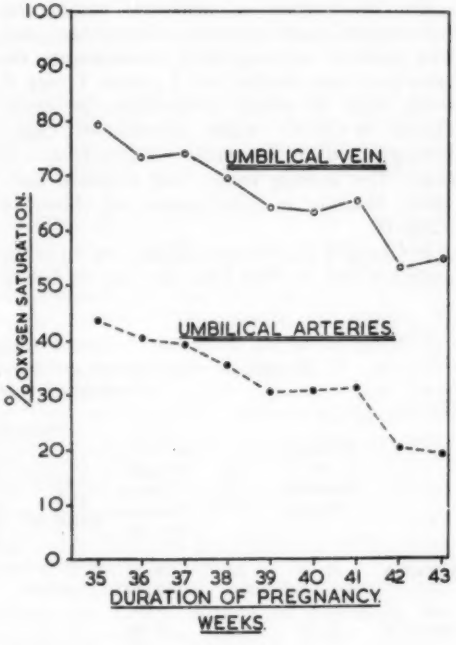


FIG. 1

Graph showing the average levels of oxygen saturation in the cord vessels from the 35th to 43rd week of normal pregnancy.

oxygen saturation falls fairly steadily from the earliest case (35 weeks) 79·1 per cent to the 10 cases at 38 weeks—69·7 per cent. At 39, 40 and 41 weeks the results are similar—64·7, 63·5 and 65·7 per cent respectively. Thereafter at 42 and 43 weeks there is a further and more marked drop to 53·5 and 55·0 per cent (see Table I).

The fall in average oxygen saturation in the umbilical arteries follows an almost identical pattern from 43·9 per cent (35 weeks) to 30·9 per cent (39 weeks), 31·0 per cent (40 weeks) and 31·8 per cent (41 weeks). At 42 weeks the average result was 20·5 per cent and at 43 weeks 19·3 per cent.

Throughout the entire group there was an almost constant arteriovenous difference in saturation of 30–35 per cent. This is also shown in the average results and is illustrated in Figure 1.

For the purpose of statistical comparison with regard to the duration of pregnancy and with patients suffering from pre-eclampsia the cases have been divided into 3 groups: Group A —less than 39 weeks (Premature)—26 cases; Group B—39–41 weeks (Term)—60 cases; Group C—over 41 weeks (Postmature)—26 cases. The average results and standard deviations obtained in these groups are shown in Table II.

In Group B the average oxygen content in the umbilical vein is 15·06 vols. per cent. In Group A the result is 1·49 vols. per cent higher (16·55 vols. per cent), and in Group C it is 2·26 vols. per cent lower (12·80 vols. per cent). Applying the "t" test to the groups, it is shown that these differences are highly significant statistically ($P<·01$). The average content in the arteries shows an almost identical pattern, the results in Groups A, B and C being 8·75, 7·31 and 4·84 vols. per cent respectively. Again the difference in levels is highly significant ($P<·01$).

In Groups A, B and C the average levels of oxygen saturation are 72·7, 64·4 and 53·9 per cent respectively in the umbilical vein, and 38·2, 31·2 and 20·2 per cent in the arteries. The fall in these levels is also highly significant (A to B, $P<·01$; B to C, $P<·01$).

The arteriovenous difference in percentage oxygen saturation is constant in the 3 groups (34·5, 33·2 and 33·7 per cent). At term the oxygen saturation in the arteries is 31·2 per cent, therefore the oxygen reserve is approximately 100 per cent.

The haemoglobin levels show a slight rise in the 3 groups as maturity increases (17·0, 17·4 and 17·8 g./100 ml.). The difference between Groups A and B is not statistically significant, nor is that between B and C ($P>·1$), but the difference between A and C (0·8 g./100 ml.) may be significant ($·1>P>·05$). There is, therefore, no significant increase in the oxygen capacity in the 3 groups, the level at term being 23·32

TABLE II

*Showing the Average Results and Standard Deviations of the Premature, Term and Postmature Groups of Normal Pregnancy*

| | Duration of Pregnancy (Weeks) | No. of Cases | Umbilical Vein | | | | Umbilical Arteries | | Arterio-venous Difference Per cent |
|---|---|---|---|---|---|---|---|---|---|
| | | | Oxygen Content Volumes Per cent | Haemo-globin g./100 ml. | Oxygen Capacity Volumes Per cent | Oxygen Saturation Per cent | Oxygen Content Volumes Per cent | Oxygen Saturation Per cent | |
| Group A | 35–38 | 26 | 16·55 ±1·14 | 17·0 ±1·1 | 22·78 | 72·7 ±4·62 | 8·75 ±0·89 | 38·2 ±4·29 | 34·5 |
| Group B | 39–41 | 60 | 15·06 ±1·70 | 17·4 ±1·4 | 23·32 | 64·4 ±4·53 | 7·31 ±1·16 | 31·2 ±4·53 | 33·2 |
| Group C | 42–43 | 26 | 12·80 ±1·60 | 17·8 ±1·9 | 23·85 | 53·9 ±5·63 | 4·84 ±1·51 | 20·2 ±6·13 | 33·7 |

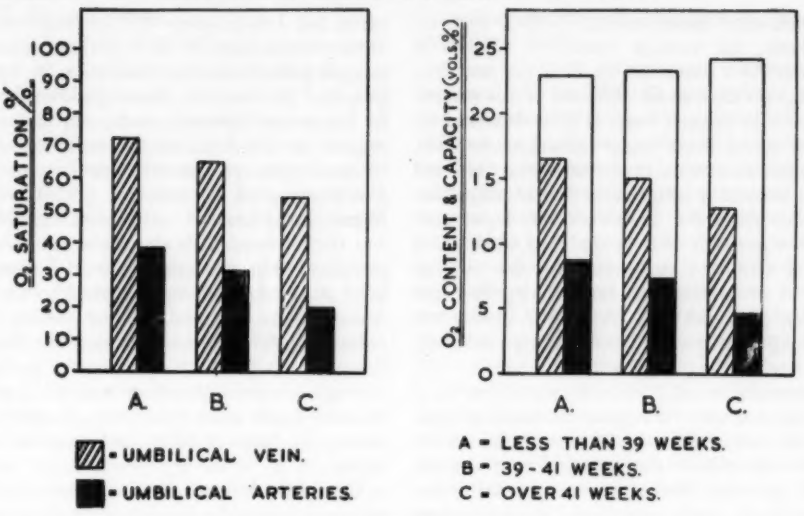


FIG. 2

Graph showing the average levels of oxygen content, capacity and saturation in the cord vessels in the premature, term and postmature cases of normal pregnancy.

vols. per cent. Thus the fall in the levels of oxygen saturation is almost entirely due to the fall in the oxygen content of the vessels. These changes are shown graphically in Figure 2.

As normal pregnancy advances from the 35th to 43rd week there is a progressive and significant fall in the average oxygen levels in the umbilical vessels at birth. There is a constant arterio-venous difference in uncomplicated cases, therefore the oxygen reserve, shown by the levels returning from the foetus, becomes progressively diminished as pregnancy advances. By 42–43 weeks, when the saturation in the arteries is 20·2 per cent, it has been reduced by fully one-third of the level shown at term (31·2 per cent). Although there is apparently an adequate supply of oxygen for foetal requirements after the 41st week, under normal conditions, there is graver danger of anoxia should any additional factor interfere with the cord circulation or the efficiency of placental oxygenation.

As already mentioned, the majority of investigations of cord oxygen levels at birth have been largely directed towards the effects of various types of anaesthesia. Particular consideration has been given to the precise duration of pregnancy and to the presence of pre-eclampsia in only a few instances. Clemetson and Churchman (1953) were concerned with the normality rather than the duration of pregnancy and in a series of 15 normal cases, delivered spontaneously and having ½ per cent Trilene for anaesthesia, the average oxygen saturation was 63·2 per cent (35·4–83·6) in the umbilical vein and 31·5 per cent (2·0–50·2) in the arteries. These results are similar to those found in the term group in this series —64·4 per cent (V—Vein), 31·2 per cent (A—Arteries). A similar technique was used in this investigation. Other average results found at spontaneous vertex delivery were Eastman (1930)—15 cases—no anaesthesia—50·5 per cent (V); Smith (1939)—21 cases—ether anaesthesia—57·1 per cent (V), 15·8 per cent (A); Watts *et al.* (1951)—8 cases—ether anaesthesia—66 per cent (V).

Walker (1953, 1954), using the Roughton and Scholander (1943) method of estimating the oxygen contents, has made a special study of the oxygen levels in the cord blood at birth with specific reference to the duration of pregnancy as well as to the normality. In a series of normal

cases delivered spontaneously (1954), with no anaesthetic, the average results of 7 cases at term were 53·7 per cent (V), 22·0 per cent (A), lower figures than those obtained in this investigation. In 18 normal cases (1953), delivered by the abdominal route under spinal anaesthesia, the oxygen saturation in the umbilical vein and arteries showed a progressive fall as pregnancy proceeded from the 21st week (66·7 per cent (V), 42·4 per cent (A)) to the 43rd week (22·6 per cent (V), 3·4 per cent (A)), the average results at 39–41 weeks (6 cases) being 56·6 per cent (V), 23·7 per cent (A), 8 per cent lower than the present series. These findings show the same trend as the present series.

Minkowski *et al.* (1953), in a study of 158 cases, showed that the highest incidence of signs of anoxia occurred in the 51 cases in which the oxygen saturation in the umbilical vein was less than 50 per cent. They also showed a fall in the oxygen levels in the cord blood in cases where pregnancy continued more than 15 days beyond the expected date of delivery.

The average haemoglobin level of 17·4±1·4 g./100 ml. in the term group compares with the results found by other investigators, e.g., Mugrage and Andresen (1936)—17·1 g./100 ml. (13–20), Guest, Brown and Wing (1938)—17·9 g./100 ml. (13–22), Mollison (1951)—16·6±1·5 g./100 ml., Walker and Turnbull (1953)—16·5 g./100 ml. (15–18·6), Marks, Gairdner and Roscoe (1955)—16·9±1·62 g./100 ml.

Walker and Turnbull (1953) have shown a progressive rise in haemoglobin level with increasing maturity and postmaturity in normal pregnancy, 9 g./100 ml. at 10 weeks, 14–15 g. at 22–24 weeks, 16·5 g. at 40 weeks and 18·8 g. at 43 weeks. Marks and his colleagues (1955), on the other hand, did not show that the highest levels recorded were associated with postmaturity. Although a slight rise with increasing maturity was shown in the average results in this study, the wide variation in the individual results tended to agree with the pattern shown by Marks.

As a conclusion to this section, the results of several cases not included in the main series are worthy of mention. Cases in which cord obstruction was present were excluded from the normal series but 7 such cases were investigated. Six of these were at term (39–41 weeks) and the average oxygen saturation was found to be 56·1 per cent (V), 11·7 per cent (A), showing a lower level than in the non-obstructed cases, particularly with regard to the level in the umbilical arteries. These figures are somewhat similar to those of Clemetson and Churchman (1953) who also found an increased arteriovenous difference, but they showed little change in the level in the umbilical vein, average results in 7 cases being 62·3 per cent (V), 5·9 per cent (A). In a further 3 cases there was undue delay during delivery caused by difficulty in delivering the shoulders, 1 case having a very short cord. In these the average oxygen saturation was 48·5 per cent (V), 14·8 per cent (A). Two of these infants were very limp at birth and required resuscitation.

Cord bloods were obtained from 7 twins (4 vertex, 3 breech) in 4 patients. As was shown by Clemetson (1956) it is difficult to compare such cases unless the type of delivery and interval between delivery of the twins is relatively constant. In the cases studied (33–38 weeks) the average oxygen saturation in all cases was much lower than in normal single pregnancy—39·7 per cent (V), 20·1 per cent (A). In the 4 vertex deliveries the average results were 41·0 per cent (V), 21·7 per cent (A), and in the 3 breech deliveries, all the second twin, 37·9 per cent (V), 18·1 per cent (A). The slightly lower figures found after breech delivery may be due to some degree of cord obstruction. The few twin pregnancies previously studied show a wide range of oxygen saturation per cent, e.g., Smith (1939)—35, 17 per cent (V), 16, 5 per cent (A); Watts *et al.* (1951)—60, 55 per cent (V). Clemetson (1956) in 6 sets of twins, normal and abnormal cases, with different types of delivery and anaesthesia showed a very wide range of 3–75 per cent (V), 1–33 per cent (A).

As was stated earlier, breech delivery is associated with cord obstruction, as well as the possibility of prolonged anaesthesia and manipulation. Only 5 cases of otherwise normal pregnancy with breech delivery were studied and the average oxygen saturation was 54·5 per cent (V), 18·7 per cent (A), both levels being lower than those found at vertex deliveries.

PART II. PRE-ECLAMPSIA

This series of 38 cases of pregnancy complicated by pre-eclampsia included both mild and severe cases. All cases showed the classical features of pre-eclampsia with elevation of blood pressure and oedema, with or without albuminuria. The moderately severe cases all showed a blood pressure of at least 150/90, oedema and albuminuria. All had an uncomplicated spontaneous vertex delivery.

These cases have been divided into 3 groups as were those of normal pregnancy: Group A—less than 39 weeks—9 cases; Group B—39–41 weeks —23 cases; Group C—over 41 weeks—6 cases. Each group is comparable with that of normal pregnancy of the same duration.

From Figure 3, showing the average levels of oxygen saturation in the cord vessels, it can be seen that these levels are lower in the cases complicated by pre-eclampsia. This is shown in all 3 groups but is most marked in the premature cases, where the average oxygen saturation in the umbilical vein is reduced by almost one-third, and in the arteries by almost one-half.

Table III shows the average results and standard deviations found in the 3 groups. Complete results are available in the thesis (MacKay, 1955).

*Group A.* In 4 severe cases, showing blood pressure 152/104–200/130, generalized oedema and albuminuria up to 8·5 g./litre, labour was induced surgically at 33–36 weeks in view of the mother's condition. Fairly heavy sedation was administered during labour. In these the average oxygen saturation was 45·1 per cent (V), 18·3 per cent (A), and the average haemoglobin 18·2 g./100 ml. In 1 severe case (38 weeks) labour was not induced. The oxygen saturation was 52·0 per cent (V), 20·7 per cent (A), and the haemoglobin 17·7 g./100 ml. The remaining 4 cases were moderately severe.

In the 9 cases the average oxygen content in the umbilical vein (11·95 vols. per cent) (see Table III) is much lower than that found in normal premature pregnancy (16·55 vols. per cent). The average oxygen saturation in the vein and arteries is also much lower, 51·2 per cent (V), 21·2 per cent (A) compared with 72·7 per cent (V), 38·2 per cent (A) in the normal cases (see Table II). Statistically, all the differences are highly significant ($P < .01$).

The arteriovenous difference (30·0 per cent)

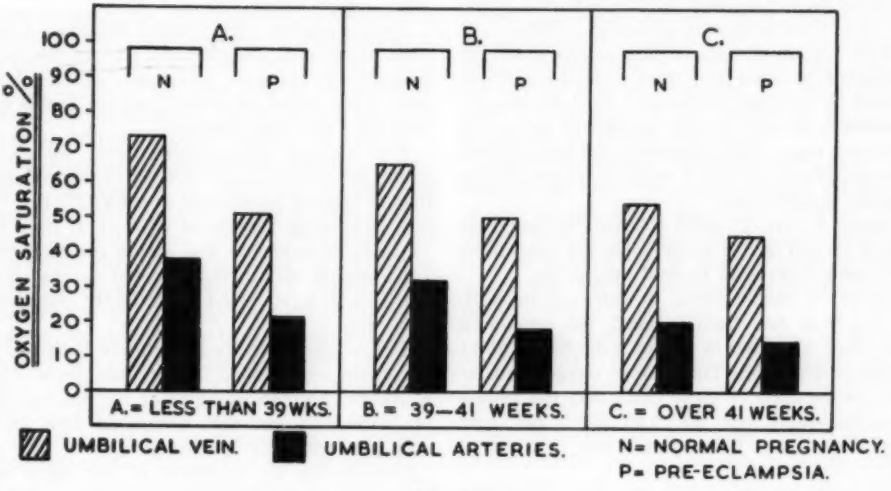


FIG. 3

Graph showing the average levels of oxygen saturation in the cord vessels of cases complicated by pre-eclampsia compared with normal pregnancy of the same duration.

TABLE III
*Showing the Average Results and Standard Deviations of the Premature, Term and Postmature Cases Complicated by Pre-eclampsia*

| | Duration of Pregnancy (Weeks) | No. of Cases | Umbilical Vein | | | Umbilical Arteries | Arterio-venous Difference Per cent |
|---|---|---|---|---|---|---|---|
| | | | Oxygen Content Volumes Per cent | Haemo-globin g./100 ml. | Oxygen Saturation Per cent | Oxygen Saturation Per cent | |
| Group A .. | 33–38 | 9 | 11·95 ±1·74 | 17·6 ±2·1 | 51·2 ±9·69 | 21·2 ±4·57 | 30·0 |
| Group B .. | 39–41 | 23 | 11·92 ±2·21 | 17·9 ±1·35 | 50·6 ±8·89 | 18·7 ±5·79 | 31·9 |
| Group C .. | 42 | 6 | 11·05 | 18·4 | 45·0 | 14·6 | 30·4 |

is almost the same as that found in normal pregnancies.

The average haemoglobin level was 17·6 g./100 ml. One patient was further complicated by being Rhesus negative with antibodies and this case showed a haemoglobin of 12·8 g./100 ml. in the cord blood. If this case is excluded from the group, the average haemoglobin is 18·2 g./100 ml. This figure shows a significant increase on the average (17·0 g./100 ml.) found in the normal premature group ($P < \cdot 05$).

The average results in this group show the greatest divergence from those of the comparable period of normal pregnancy but, as already indicated, all were at least moderately severe. In addition, signs of pre-eclampsia had been present for some time, at least 3 weeks in all except the Rhesus negative case.

*Group B.* The 23 cases (9 mild, 10 moderate and 4 severe) in this group form the main basis for comparison with normal pregnancy.

Of the 4 severe cases, 3 were non-booked. In 3 labour had been induced, the remaining one being admitted in labour. One had a fit 11 hours post-partum. The average oxygen saturation in the cord in these cases was the lowest recorded—42·8 per cent (V), 17·0 per cent (A). The average haemoglobin was 18·4 g./100 ml.

In the 23 cases, the average oxygen content in the umbilical vein (11·92 vols. per cent) is much lower than the average level found in normal cases at term (15·06 vols. per cent) (see Tables II and III). The average oxygen saturation in both vessels 50·6 per cent (V), 18·7 per cent (A) is also lower than in the normal term group, where the levels were 64·4 per cent (V), 31·2 per cent (A). The highest level recorded in the umbilical vein was only 59·6 per cent.

The reduction in the average oxygen levels, compared with those of normal pregnancy, is again highly significant ($P < \cdot 01$).

Once more the arteriovenous difference is just over 30 per cent, therefore the oxygen reserve is considerably reduced, being only about 60 per cent as the blood returning from the foetus was only 18·7 per cent saturated.

The average haemoglobin level was 17·9 g./100 ml. The increase in level, compared with that of normal pregnancy at term (17·4 g./100 ml.) is possibly significant ($P \sim \cdot 1$). If only the 14 cases of moderate and severe pre-eclampsia are included, the increase in the average level ($18 \cdot 2 \pm 1 \cdot 2$ g./100 ml.) is certainly significant ($P < \cdot 05$).

The oxygen capacity is therefore increased in the cases complicated by pre-eclampsia, 18·2 g./100 ml. corresponding to an oxygen capacity of 24·39 vols. per cent compared with 23·32 vols. per cent in the normal group.

Considering the duration of the signs and symptoms of pre-eclampsia, without regard to the severity of the condition, there were 6 cases of a duration of less than 3 weeks. These cases

included 1 severe and 3 moderate, and all had been attending the antenatal clinic regularly so the time of onset of toxaemia was fairly accurately known. It is interesting to note that the average oxygen saturation in the umbilical vein in the 6 cases was 56·5 per cent (52·5–59·6) compared with 48·5 per cent (26·8–57·9) in the remaining 17 cases. The group of 6 cases is rather small for statistical analysis but, applying the "t" test to the groups, $P < \cdot 05$, which is significant.

The average haemoglobin levels were 17·5 g./100 ml. in the 6 cases of short duration and 18·0 g./100 ml. in the remainder.

There is, therefore, a significant diminution in the average levels of oxygen saturation and content in the umbilical vessels in cases complicated by pre-eclampsia. The order of this diminution appears to be dependent not only on the severity of the toxaemia but also on its duration. The arteriovenous difference found after spontaneous vertex delivery is fairly constant and of the same order as that found in normal pregnancy.

There is a significant increase in haemoglobin level in the cases of pre-eclampsia, with the possible exception of mild cases and those of short duration. As was suggested by Walker and Turnbull (1953), this increase in haemoglobin is probably a response of the foetus to a falling oxygen supply. They also showed an increased level of haemoglobin in pre-eclampsia although this was not confirmed by Marks *et al.* (1955).

The average oxygen levels shown are also similar in pattern to those of Walker and Turnbull (1953), who found an average oxygen saturation of 23·7 per cent (V), 7·4 per cent (A) in 5 severe cases of pre-eclampsia (34–39 weeks), delivered by Caesarean section under spinal anaesthesia. In 1 moderate case (37 weeks), delivered spontaneously they recorded readings of 46·8 per cent (V), 20·8 per cent (A). The levels in both vessels were lower than those found in normal pregnancy.

Clemetson and Churchman (1953), in their study of cases complicated by pre-eclampsia, found a completely different type of result. The average results of 5 cases, delivered spontaneously, were 62·3 per cent (V), 16·1 per cent (A). These showed no reduction in the oxygen level in the vein but a marked increase in the arteriovenous difference, similar to the results obtained in normal pregnancy with cord obstruction—62·3 per cent (V), 5·9 per cent (A). This led to their suggestion that there might be a slowing of the foetal umbilical circulation in cases complicated by pre-eclampsia, a suggestion which is not confirmed by the present investigation.

In 4 cases of Group B (3 moderate and 1 severe) labour was induced by artificial rupture of the membranes. In these cases the oxygen saturation in the umbilical vein was relatively high—52·4, 54·8, 59·2 and 59·6 per cent.

*Group C.* Five of the 6 cases in this group were classified as mild, the remaining case being moderately severe. The latter was non-booked and had labour induced on the day following admission.

The average results are again shown in Table III but standard deviations have been excluded as this group is rather small for statistical analysis. The average oxygen saturation in the umbilical vein (45·0 per cent (35·1–56·3)) is almost the lowest recorded. The only comparable figures are the average results found in severe cases (45·1 per cent in the premature group, 42·8 per cent at term). The average oxygen content in the vein was 11·05 vols. per cent, compared with 12·80 vols. per cent in the normal postmature group. The haemoglobin level was 18·4 g./100 ml., compared with 17·8 g./100 ml. in the normal cases.

The arteriovenous difference is again just over 30 per cent, the average oxygen saturation in the arteries being only 14·6 per cent. This means that the oxygen reserve is less than one-half of that shown in normal cases at term, where the average oxygen saturation in the arteries was 31·2 per cent.

Although the majority of the cases were mild, they were of at least 3-weeks duration. It can be suggested, therefore, that in cases complicated by pre-eclampsia, however mild, allowed to continue beyond the 41st week there is an even more marked fall in the oxygen levels in the umbilical cord. As was shown in the normal series, there is apparently an adequate supply of oxygen under normal conditions of uncomplicated vertex delivery, but a much graver

danger of anoxia should any complication arise.

A few cases complicated by hypertension have been studied but the results are at present incomplete. Further cases are to be investigated before the drawing of any definite conclusions.

## Part III. Instrumental and Operative Deliveries

This group of cases (15 forceps deliveries, 38 Caesarean sections) has been included merely to show some of the results obtained. In view of the variable factors associated with each case, e.g., (*a*) indication for delivery, (*b*) the type and degree of anaesthesia, (*c*) the anaesthetist, (*d*) the induction of anaesthesia–delivery interval, (*e*) difficulty encountered during delivery, such as uterine contraction during section, etc., no attempt is made at statistical analysis or comparison. Figures are given for the percentage oxygen saturation in the umbilical vein.

It is not suggested that these results of oxygen levels in the umbilical cord at birth give a true picture of the conditions *in utero* but it is certain that at birth the infants were frequently being exposed, however momentarily, to a very low supply of oxygen which might, if prolonged, have endangered life. In many cases the oxygen reserve was minimal. This might have been due to the delivery or to the anaesthetic or to some associated factor.

### A. *Forceps Deliveries*

Five cases had a normal pregnancy and were delivered under general anaesthesia (40–41 weeks). The average oxygen saturation in the umbilical vein was 55·8 per cent (31·3–81·8). Two cases showing foetal distress had a saturation of 31·3 and 47·8 per cent. The low level of 31·3 per cent was also associated with the administration of nitrous oxide, shown by Eastman (1936, 41·3 per cent), Smith (1939, 32·6 per cent) and Taylor, Govan and Scott (1951, 43·4 per cent) to be associated with lower than normal levels of oxygen in the cord blood.

Nine cases were complicated by varying degrees of pre-eclampsia and were delivered under various types of general anaesthesia (37–42 weeks). The average oxygen saturation in the umbilical vein was 43·9 per cent (12·7–70·5). Again a very wide range of results is shown but it is interesting to note that: (1) the average result is considerably lower than that found after spontaneous vertex delivery in normal (64·4 per cent) or pre-eclamptic (50·6 per cent) cases at term although only 1 case was classified as severe pre-eclampsia, (2) foetal distress was associated with a recording of 41·0 per cent and (3) nitrous oxide was administered in the cases showing levels of 12·7, 41·0, 48·0 and 50·5 per cent.

Other investigators have shown varying average results in cases delivered by forceps. Eastman (1936) in 8 cases of low forceps delivery with ether anaesthesia found an average of 45 per cent and Watts *et al.* (1951) in 17 cases of low forceps with ether anaesthesia 68 per cent. Clemetson and Churchman (1953) in 7 forceps deliveries, having the same anaesthetist and anaesthetic, found a wide variation of results, e.g., 3 normal cases, 68·7 per cent (66·3–72·7), 2 cases of pre-eclampsia, 59·6 per cent (44·5–74·8).

### B. *Caesarean Sections*

Of this group (38 cases), 13 were normal pregnancies, 10 complicated by pre-eclampsia and 13 by diabetes mellitus.

In this series an even greater number of factors influence the results, e.g., type of section, whether or not elective, state of uterine tone at delivery, etc.

Full results are also recorded elsewhere and here again only some of the readings of the percentage oxygen saturation in the umbilical vein are included.

(1) *Normal Pregnancy*. Of 10 elective sections, 9 were lower segment operations and 1 classical. In 7 lower segment sections (39–40 weeks) delivered under general anaesthesia the average oxygen saturation was 35·6 per cent (21·2–64·1) and in 1 case (42 weeks), again having general anaesthesia, 33·7 per cent. Nitrous oxide was administered as part of the anaesthetic in 4 cases—31·8, 32·4, 33·7 and 40·6 per cent. One case (known duration 44 weeks) was delivered under local anaesthesia—37·4 per cent. There was little liquor and marked yellow staining. In the case delivered by classical

section (39 weeks) under general anaesthesia the result was 57·8 per cent.

Of 3 cases, in labour when lower segment section was performed, 2 (38, 41 weeks) had general anaesthesia—68·3, 35·3 per cent, and 1 (40 weeks) spinal with oxygen—73·7 per cent.

Again a very wide range of results is shown with many very low readings. The average of the 13 cases was 42·7 per cent, well below that found at spontaneous vertex deliveries.

Clemetson and Churchman (1953) in 4 cases showed an average of 43·1 per cent (27·8–66·1). Walker and Turnbull (1953) in a series of normal cases delivered under spinal anaesthesia with no oxygen recorded 56·6 per cent (52·8–61·3) in 6 cases at 39–41 weeks. Dieckmann and Kramer (1944), by serial sampling, showed an increase in the oxygen levels in the cord during the administration of oxygen to the mother. The highest record in this group (73·7 per cent) was associated with the administration of oxygen during spinal anaesthesia.

(2) *Pre-eclampsia.* Of 5 elective sections, 1 was classical (35 weeks) and had general anaesthesia —50·7 per cent. Three severe cases (32–36 weeks) were delivered by lower segment operations under spinal anaesthesia—23·5, 37·7 and 50·5 per cent. One moderately severe case (38 weeks) was delivered by lower segment operation under general anaesthesia—46·9 per cent.

Five cases (3 mild, 2 severe) were in labour when lower segment section was carried out. All had general anaesthesia: 1 (38 weeks)—33·3, 1 (40 weeks)—18·8, 1 (41 weeks)—58·6, 2 (42 weeks)—13·9, 26·1 per cent.

All the results are low; the highest (58·6 per cent) was from a case of mild toxaemia and this was the only infant in really good condition at birth. In the cases showing the lowest levels (13·9, 18·8, 23·5, 26·1 and 33·3 per cent) the infants were very limp and signs of foetal distress were present before delivery in 2 of the cases.

Nitrous oxide was administered in 2 of these cases—13·9 and 33·3 per cent.

Clemetson and Churchman (1953) in 3 cases of severe pre-eclampsia delivered by section obtained results of 5·9–26·2 per cent. All the mothers were fully oxygenated.

Walker and Turnbull (1953) in 5 cases of severe pre-eclampsia found a similar result: 10·5–32·5 per cent.

(3) *Diabetes Mellitus.* All 13 cases had elective sections and 3 showed a mild degree of superimposed toxaemia.

Of 3 classical sections, 2 (35–36 weeks) were delivered under general anaesthesia—34·2, 71·6 per cent, and 1 (37 weeks) under spinal—59·8 per cent.

Of the 10 lower segment operations, all of whom had spinal anaesthesia, 7 showed no signs or symptoms of pre-eclampsia. In these cases (35–38 weeks) the average oxygen saturation was 33·0 per cent (11·0–60·2). The remaining 3 cases (36 weeks) showed an average of 28·9 per cent (11·0–44·6).

The average of the 13 cases was 37·1 per cent. This figure and the majority of the individual results are extremely low, with practically no oxygen returning from the foetus in many cases. Again the range of results is wide.

Oxygen was administered during the operation in 2 cases—60·2, 11·0 per cent. The former is one of the highest levels in the group. In the latter there was some delay at delivery caused by a uterine contraction.

In the few cases studied, the results obtained at classical Caesarean section appear to be higher than those of lower segment deliveries: normal (1 case)—57·8 per cent, pre-eclampsia (1 case)—50·7 per cent, diabetes mellitus (3 cases)—34·2, 59·8 and 71·6 per cent.

## Discussion

We have already discussed the average cord oxygen saturations obtained in this work and by other authors. Our figures amply confirm those of Walker and Turnbull (1953) that there is a gradual reduction in the oxygen levels of the cord blood in *normal pregnancy* as term is approached and passed, although the actual figures obtained by these authors are somewhat lower than those found by us and other workers in this field. Thus at the 43rd week of pregnancy we find that there is still some oxygen reserve left but not a great deal. Some authors are of the opinion that other techniques of sampling and other methods of delivery give a more accurate picture of the cord oxygen levels *in utero*. Nesbitt (1955), for instance, has suggested that

reliable figures can only be obtained by sampling the cord before the delivery of the child at classical Caesarean section performed under local anaesthesia. Such a procedure would be difficult to justify for we are not attempting to establish the precise intra-uterine conditions before the onset of labour but rather trying to obtain an overall picture of the intra-uterine and intra-partum transfer of oxygen from mother to foetus. In *pre-eclampsia* the cord oxygen levels are reduced below those corresponding to the appropriate period of normal pregnancy. Perhaps one of our most important observations is that the duration of the toxaemia as well as its severity affects the cord oxygen levels. This point is well known to the clinician and the small baby associated with a long-continued mild toxaemia may be in much greater jeopardy than another whose mother is suffering from an acute explosive toxaemia of short duration. In our own series the infant who is in a very dangerous situation is one whose mother has been suffering from a long-continued mild toxaemia and who is allowed to become postmature. The cord oxygen levels in these cases may be truly desperately low. In Part III we have described the cord oxygen figures obtained under various conditions of anaesthesia and types of operative delivery. General anaesthesia is nearly always associated with a reduction in the cord blood oxygen content and, as has been frequently noticed before, nitrous oxide is a particularly dangerous anaesthetic in this respect. The cord oxygen saturation in the diabetic series is noteworthy and the comparatively low saturations recorded indicate how precarious is the diabetic infant's life, in many cases even at the 36th week of pregnancy.

Little is known of the factors governing the blood supply to the uterus and the placenta in health and disease. Metcalfe and his co-workers (1955) have recently adduced evidence that the blood supply to the uterus in late pregnancy is of the order of 500 ml. per minute, but so far they have not recorded flows determined in postmature or pre-eclamptic pregnancies. If the blood flow in the myometrium reflects the blood supply to the whole uterus and its contents, then the work of Morris, Osborn and Payling Wright (1955) would suggest that there is a serious reduction of blood flow to the uterus in pre-eclampsia. Moore and Myerscough (1957) who have confirmed this work have shown, in addition, that there is a marked slowing of the clearance rate as term is passed and the patient becomes postmature. Browne and Veall (1953) in their well-known work were the first to demonstrate that there was a reduced clearance rate in the chorio-decidual space in the pre-eclamptic as compared with the normal woman. It is widely believed that this lowered blood flow to the placenta is associated with a degeneration of the placental membrane. The increase in fibrin nodes has often been commented on but seldom expressed quantitatively. It is presumably owing to a degeneration in the membrane that oxygen ceases to pass so readily to the foetus. The chorion is supplied with about 400 arterioles, but little is known about their precise anatomy and virtually nothing of any pathological change which might occur in pre-eclampsia or in senescence. Whether or not it is a pathological change in these vessels which determines the fall in blood flow to the placenta is unknown.

It is unnecessary here to stress the clinical lessons that can be learned from a knowledge of the presumptive cord oxygen saturations at certain stages of normal and abnormal pregnancy. That there is still some oxygen reserve for the foetus even at the 43rd week of pregnancy is probably true in most cases and a straightforward labour with a spontaneous delivery would not perhaps lead to any serious anoxia of the infant; an abnormal labour in such a patient and in particular a forceps delivery with an indifferently given anaesthetic may spell disaster for the infant. As far as pre-eclampsia is concerned a knowledge of the cord oxygen levels once again emphasizes that in many cases it is much better to induce labour than to allow the infant to continue an intra-uterine existence in an undesirable environment.

## Conclusions

(1) The arteriovenous difference in percentage cord oxygen saturation from the 35th to 43rd week of normal pregnancy is 30–35 per cent.

(2) There is a progressive fall in the cord

oxygen levels as pregnancy matures to term and thereafter, the oxygen reserve at term being about 100 per cent.

(3) In pre-eclampsia there is an arteriovenous difference in percentage oxygen saturation of the same order as that found in normal pregnancy.

(4) Compared with the average results found in normal pregnancy there is a fall in cord oxygen levels in cases complicated by pre-eclampsia, the average oxygen reserve at term being about 60 per cent. The order of this reduction is related to the duration of the disease as well as to its severity.

(5) There is an increase in the haemoglobin level in the cord blood in most cases complicated by pre-eclampsia.

(6) In instrumental and operative deliveries results are presented showing a very wide range but on the whole demonstrating the deleterious effect of these procedures on the transfer of oxygen from the mother to the foetus.

## Acknowledgments

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## References

Arnold, P. (1949): *Bull. Inst. med. Lab. Tech.*, **14**, 137.
Barcroft, J., Kennedy, J. A., and Mason, M. F. (1940): *J. Physiol.*, **97**, 347.
Browne, J. C. M., and Veall, N. (1953): *J. Obstet. Gynaec. Brit. Emp.*, **60**, 141.
Clemetson, C. A. B., and Churchman, J. (1953): *J. Obstet. Gynaec. Brit. Emp.*, **60**, 335.
Clemetson, C. A. B. (1956): *J. Obstet. Gynaec. Brit. Emp.*, **63**, 1.
Dieckmann, W. J., and Kramer, S. (1944): *Proc. Soc. exp. Biol., N.Y.*, **55**, 242.
Eastman, N. J. (1930): *Bull. Johns Hopk. Hosp.*, **47**, 221.
Eastman, N. J. (1936): *Amer. J. Obstet. Gynec.*, **31**, 563.
Guest, G. M., Brown, E. W., and Wing, M. (1938): *Amer. J. Dis. Child.*, **56**, 529.
MacKay, R. B. (1955): *Studies on the oxygenation of the foetus in normal and abnormal pregnancy.* M.D. Thesis. University of Edinburgh.
Marks, J., Gairdner, D., and Roscoe, J. D. (1955): *Arch. Dis. Childh.*, **30**, 117.
Metcalfe, J., Romney, S. L., Ramsey, L. H., Reid, D. E., and Burwell, C. S. (1955): *J. clin. Invest.*, **34**, 1632.
Minkowski, A., Caillebotte, N., Ste.Anne-Dargassies, S., Larroche, J. C., Barab, R., and Maille, G. (1953): *Études néonat.*, **2**, 197.
Mollison, P. L. (1951): *Blood transfusion in clinical medicine.* Blackwell, Scientific Publications, Oxford. p. 352.
Moore, P. T., and Myerscough, P. R. (1957): In press.
Morris, N., Osborn, S. B., and Wright, N. P. (1955): *Lancet*, **1**, 323.
Mugrage, E. R., and Andresen, M. I. (1936): *Amer. J. Dis. Child.*, **51**, 775.
Nesbitt, R. E. L., Jr. (1955): *Obstet. Gynec. Surv.*, **10**, 311.
Orcutt, F. S., and Waters, R. M. (1937): *J. biol. Chem.*, **117**, 509.
Roughton, F. J. W., and Scholander, P. F. (1943): *J. biol. Chem.*, **148**, 541.
Smith, C. A. (1939): *Surg. Gynec. Obstet.*, **69**, 584.
Taylor, E. S., Govan, C. D., and Scott, W. C. (1951): *Amer. J. Obstet. Gynec.*, **61**, 840.
Van Slyke, D. D., and Neill, J. M. (1924): *J. biol. Chem.*, **61**, 523.
Walker, J., and Turnbull, E. P. N. (1953): *Lancet*, **2**, 312.
Walker, J. (1954): *J. Obstet. Gynaec. Brit. Emp.*, **61**, 162.
Watts, J., Henderson, H., Kaump, D. H., and Davis, R. M. (1951): *Amer. J. Obstet. Gynec.*, **61**, 1025.

# CANCER OF THE UTERINE CERVIX: SOME COMMENTS ON EARLIER DIAGNOSIS

BY

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CARCINOMA of the cervix is usually squamous in nature. It is logical to assume that the neoplastic change begins in the epithelial cells themselves and that infiltration of the subjacent stroma occurs later; in other words, an intra-epithelial phase precedes the invasive stage. While the lesion remains confined to the epithelium it is detected only by chance or as the result of some screening procedure. After invasion has occurred, symptoms such as bleeding do not necessarily follow at once; much depends on the surface extent of the lesion and its tendency to ulcerate, and on whether or not the cervix is subjected to trauma.

It is convenient to discuss three somewhat arbitrary phases in the development of the cancer: (1) intra-epithelial, (2) invasive but producing no characteristic clinical features and (3) invasive with pathognomonic signs and symptoms. Treatment is likely to prove more effective the earlier it is applied in the evolution of the disease, and indeed earlier diagnosis should contribute more to improving survival rates than advances in methods of treatment. There is, however, a distinct danger that in the search for the earliest evidence of cancer some epithelial abnormalities may be regarded and treated as malignant on inadequate grounds. The only criterion of success in the diagnosis and treatment of supposedly pre-invasive lesions is a reduction in both the incidence and the mortality rates from cancer of the cervix in the years to come.

This question of earlier diagnosis will be discussed in the light of experience in the Aberdeen area. Attention will be centred in turn on the three phases previously mentioned, but it must be emphasized that a vitally significant factor remains unknown—the time relationship of these phases. There is no means of determining when the epithelium first becomes malignant or when invasion begins. The intra-epithelial stage may be protracted—an average duration of 10 years or more has been suggested; on the other hand, in some cases it may well be transient, affording little opportunity for detection. Once the lesion has become invasive, the time of onset of typical symptoms depends on its rate of growth, its site and superficial extent and its exposure to trauma. A patient with irregular bleeding for many months may present a localized tumour, another who reports almost immediately may have malignant infiltration throughout the pelvis.

## INVASIVE CANCER WITH CHARACTERISTIC SIGNS AND SYMPTOMS

It is as well to start with the situation as it actually presents to the gynaecologist. The overall survival rate for any series is largely pre-determined by the relative proportion of favourable to advanced cases it contains. In a previous report (Lawson, 1956) attention was drawn to the unreliability of classification by clinical stages but nevertheless the grouping of cases according to the local extent of the tumour does afford the most satisfactory means to date of assessing prognosis. According to the majority of British centres which publish reports, between 55 and 65 per cent of all cases are in Stages I and II when first seen. Survival rates at 5-years for all cases seen vary from about 30 to 40 per cent, ranging from 50 to 60 per cent for Stage I to virtually nil for Stage IV. Obviously an increase in the proportion of Stage I and II cases will lead to an improvement in the overall survival rates.

Distribution by clinical stages varies so

markedly, however, from centre to centre that it is convenient to approach the matter from another angle, namely by correlating survival rates with the duration of symptoms prior to treatment. Goldscheider and Stern (1955) have stated that "patients with the disease in a later stage have in general had a longer history than those with the disease in an earlier stage" and "for each stage a short delay of up to 6 months is positively correlated with a short survival time of less than 2 years". The fact that patients with a long history often do better than those with a short history does not, however, constitute an argument against the value of earlier diagnosis. An advanced lesion must have progressed from an earlier stage, and even in the case of slow-growing neoplasms earlier treatment would presumably have proved still more effective. Way (1951) has shown that his best results were obtained in patients seeking treatment between 6 and 12 months after the onset of symptoms. Those reporting within 6 months included many with rapidly-progressive tumours, whereas when the delay was a year or more the proportion of advanced lesions was increased. Donaldson (1955) is of the opinion that dividing any series into those delaying less and those delaying longer than 6 months achieves in effect a comparison between two different types of neoplasm; the former group includes all patients with rapidly-spreading, anaplastic growths, whereas women in the latter category have only well-differentiated, slowly-progressive lesions. He believes that a more refined analysis, assessing survival rates for those delaying 0 to 1, 1 to 2, and 2 to 3 months before seeking advice, would show that in general the shorter the delay the better the prognosis.

During the 12 years 1942 to 1953, 552 cases of cervical cancer were dealt with in the Gynaecological and Radiotherapy Departments of Aberdeen Royal Infirmary. A positive correlation has been found between clinical stage and duration of symptoms prior to diagnosis. Patients with Stage I lesions delayed on the average just over 5 months, Stage II—a little over 6 months, Stage III—almost 7 months, and Stage IV—nearly 10 months, with an overall average of just on 6 months. For individual cases in each stage the actual delay ranged from a few days to 2 years or more, but a shorter overall average delay should produce a more favourable stage distribution.

Survival rates have also been calculated in relation to duration of symptoms. During the period 1942 to 1947, 253 cases were seen and of these 68 were alive 5 years later (26·9 per cent), Table I showing details for the individual stages.

TABLE I

*Survival Rates for All Cases Seen During 1942–1947*

(Percentage figures in parentheses)

| Clinical Stage | Total | Died Within 5 Years | Outcome Unknown | Alive at 5+ Years |
|---|---|---|---|---|
| I .. .. | 42 | 15 | 4 | 23 (54·8) |
| II .. .. | 112 | 74 | 5 | 33 (29·5) |
| III .. .. | 71 | 57 | 2 | 12 (16·9) |
| IV .. .. | 28 | 28 | 0 | 0 |
| Total .. .. | 253 | 174 | 11 | 68 (26·9) |

Of the 253 women, 86 attended within 3 months of the onset of symptoms and of these 29 (33·7 per cent) survived for 5 years; of the 167 delaying longer than 3 months, only 39 (23·4 per cent) survived for a similar period (Table II). The difference in survival rates is mainly due to the fact that 73 of the 99 Stage III and IV cases were in the group with the longer duration of symptoms. Further subdivision of the cases according to clinical stage yields the following information: of 60 Stage I and II cases attending within 3 months, 23 survived for 5 years (38·3 per cent), and of 94 Stage I and II cases reporting after 3 months, 33 lived for 5 years (35·3 per cent); of 26 Stage III and IV cases seen within 3 months, 6 were alive 5 years later (23·1 per cent), and of 73 Stage III and IV cases delaying more than 3 months, only 6 survived 5 years (8·2 per cent).

Provided the disease is still in Stage I or II when treated, the extent of the delay appears, therefore, to have comparatively little influence on the outcome. If, however, the cancer is advanced when the patient is first seen, the prospect of survival is closely related to the duration of symptoms. These points support the opinion that there are probably two main forms

TABLE II
*Survival Rates for All Cases Seen During 1942–1947, Correlated With Duration of Symptoms*
(Percentage figures in parentheses)

| Clinical Stage | Duration of Symptoms | | | | All Cases | | |
|---|---|---|---|---|---|---|---|
| | 3 Months or Less | | Over 3 Months | | No. | Survival | |
| | No. | Survival | No. | Survival | | | |
| I .. .. .. | 15 | 9 (60·0) | 27 | 14 (51·9) | 42 | 23 | (54·8) |
| II .. .. .. | 45 | 14 (31·1) | 67 | 19 (28·5) | 112 | 33 | (29·5) |
| III .. .. .. | 21 | 6 (28·6) | 50 | 6 (12·0) | 71 | 12 | (16·9) |
| IV .. .. .. | 5 | 0 (0·0) | 23 | 0 (0·0) | 28 | 0 | (0·0) |
| Total .. .. | 86 | 29 (33·7) | 167 | 39 (23·4) | 253 | 68 | (26·9) |

of cervical cancer: a slowly-progressive type tending to remain localized to the cervical region, and here some delay may not be of serious consequence; and a more malignant variety probably metastasizing readily to the regional lymph nodes and amenable to therapy only if treated without delay. The relative frequency of the two types in any representative series is impossible to determine but it would seem that the chief advantage in reducing the average duration of symptoms prior to treatment would be to improve the prognosis for a limited number of highly-malignant cases. Although the resultant improvement in survival rates would be difficult to detect statistically, some attention should be paid to the means whereby women can be induced to report sooner.

Aitken-Swan and Paterson (1955), in discussing the reasons why cancer patients defer seeking advice, describe two groups: those who "know" they may have cancer, and those who are quite unaware of the possible cause of their symptoms. The former group includes those who are afraid to have their suspicions confirmed and others who adopt a fatalistic attitude in the belief that nothing can be done. Those who are ignorant of the possibilities tend to seek advice sooner for their actions are governed solely by the inconvenience of their symptoms, and it is to this group that most cervical cancer patients belong. Cancer propaganda might, therefore, convert the delay of ignorance into the longer delay incurred by fear.

As far as cervical cancer is concerned, indirect pressure may well prove more helpful than any specific programme of cancer education. If the family doctor never omits to perform vaginal examination when the complaint is of irregular bleeding, a certain number of cancers will be detected sooner than would otherwise have been the case; perhaps more important, the fact that the medical profession regards such bleeding, especially at the menopause, as worthy of investigation should do much to dispel the impression amongst the laity that it is a natural phenomenon. Such a policy need not cause alarm for in the majority of cases causes other than cancer will be found and treated; in the few discovered, however, to have malignant disease, treatment can be given at a time when it is more likely to prove effective. Nevertheless, it is doubtful if efforts aimed at reducing delay in starting treatment after the onset of symptoms are likely to contribute any striking improvement in survival rates. Attempts must rather be directed to detecting the disease before pathognomonic features have arisen.

### Invasive Cancer Without Characteristic Signs and Symptoms

Invasive cancer must presumably have been present for some time, long or short, before superficial ulceration leads to bleeding. Recently, for example, an unsuspected invasive squamous carcinoma was found in a uterus removed in Aberdeen for pelvic pain, the patient denying any abnormal haemorrhage. The lesion had apparently originated from a very small area but had widely infiltrated the cervical substance beneath a shell of intact healthy squamous

epithelium. The female population must contain a number of such women in whom invasive cancer is established but who have not developed typical clinical features. If gynaecological advice is sought for any reason at all, it should be possible to detect the presence of the cancer. In some instances, careful questioning will elicit the hitherto undisclosed information that post-coital "spotting" has occurred on occasion. In others, bleeding on examination or friability on applying the vulsellum may point the way to the correct diagnosis. Where the history is not suggestive and ordinary clinical examination is negative—as in the case mentioned above—special procedures such as cytology may indicate the need for histological investigation. Schiller's test, colposcopy, cytology, and the "office biopsy" of the Americans have all proved successful in bringing to light cases of cervical cancer which would otherwise have been overlooked, and some authorities believe that even if only an occasional case is detected some form of routine screening is worth while. The detection of intra-epithelial lesions must, of course, also be taken into account in assessing the value of these techniques, but for the moment consideration will be restricted to latent but invasive neoplasms, the malignant nature of which is not in doubt.

Aberdeen City has a population of some 185,000 persons (1951 Census), of whom about 52,000 are married women (including widowed and divorced), aged 20 years and over. During the 12-year period 1942 to 1953, 255 cases of cervical cancer occurred in women resident in the City, 245 being married women aged 20 years and over. The number of new cases occurring each year in married women is very close to the calculated annual average of 20, and it would seem, therefore, that at any given date there are approximately 20 married women in the City who will appear within a year with cancer of the cervix. To detect these 20 cases prior to the onset of symptoms, however, it would be necessary to examine each year over 50,000 women—and account would also have to be taken of changes in number and composition due to ageing, deaths and new marriages. The situation is further complicated by the possibility that some lesions may evolve rapidly and others slowly. A woman with the former type of neoplasm might have been thoroughly investigated with quite negative results a few months or even weeks before she appeared as a clinical case of cervical cancer; another case might, of course, be detected a year or more before symptoms would have appeared.

If particularly susceptible groups of women could be selected for examination, the chances of detecting unsuspected lesions should be correspondingly greater. Analysis of the Aberdeen City cancer data has shown that 8 of the 20 annual new cases will occur among the 7,000 women aged 45 years and over who have had 4 or more viable pregnancies, while approximately 4 of the 20 cases will occur among the 1,600 women aged 45 years and over who have had 7 or more viable pregnancies. If, for example, it were feasible annually to screen all women in the latter category, 1 cancer in 5 of the annual total of cases, that is 4 out of 20, should theoretically be detected somewhat sooner than in the natural course of events. Although this would presumably exert some effect on the overall clinical stage distribution, any influence on the survival rates would almost certainly be very slight. One must also bear in mind that women of high parity are as a rule drawn from the lower social groups and are least likely to take advantage of any facilities offered for routine examination.

In so far as the screening of gynaecological patients rather than the general female population is concerned, the following points are of interest. Of 552 cases of cervical cancer seen during a 12-year period, 36 (6·5 per cent) gave a history of previous gynaecological consultation; 16 had been seen within 5 years of the diagnosis of cancer, and another 9 between 5 and 10 years previously, so that 25 in all had been seen within 10 years. Taking the actual dates of the previous consultation into account, it can be calculated that of the 5,000 women seen each year by the Aberdeen gynaecological staff, 2 will re-appear within 10 years with invasive cancer of the cervix. Expressed in another way, it may be said that of the 50 or so new cases which occur annually in the North-Eastern Region, only 2 will have received previous gynaecological attention. Detailed study of the

case records of each of the 25 patients concerned suggests that in about 50 per cent clinical judgment was faulty—significant symptoms were ignored or a frankly unhealthy cervix was not submitted to biopsy. As regards the others, it may be that in some intra-epithelial carcinoma was already present when the patient was first seen and that this might have been diagnosed had a biopsy been taken. It may be argued that routine cytology or some other procedure would provide a useful check on human fallibility but a very considerable amount of negative work would have to be undertaken.

### Intra-epithelial Cancer

In theory a much more positive gain is to be expected if the net is cast so as to discover cases before invasion occurs. Intra-epithelial cancer or carcinoma *in situ* has been defined as an epithelial lesion presenting all the criteria of malignancy except invasion of the underlying stroma. Unfortunately experts differ on the interpretation of any given case, and moreover, as Younge (1939) has pointed out, histological evidence is not sufficient to prove a direct relationship between such intra-epithelial changes and invasive cancer; clinical and statistical experience must support the contention that the superficial lesion is the progenitor of invasive carcinoma.

There is ample evidence that some lesions conforming to the criteria of carcinoma *in situ* have in the course of time evolved into invasive cancer but that some cases behave in this way does not warrant the assumption that all do so. Besides, in the majority of established cancers there is no means of telling whether or not there was an intra-epithelial phase of significant duration.

Galvin, Jones and TeLinde (1952) were able to trace histological material previously obtained from 21 of 723 cases of cervical cancer. Evidence of carcinoma *in situ* was found in 11 of 13 previous biopsies and in 2 of 8 previous curetted specimens. The intervals involved ranged from 1 to over 16 years, with an average of 8 years. In the Aberdeen series of 552 cases curetted material was traced for 11 patients, and 5 of the specimens contained cervical as well as endometrial tissue; in 2 cases aberrant squamous epithelium was identified on review. In none of the Aberdeen cases was previous cervical biopsy material available for study.

In the light of their experience, Galvin and his associates state: carcinoma *in situ* is potentially invasive; clinical cancer is preceded by intra-epithelial carcinoma oftener than would occur by chance; the pre-invasive phase constitutes the greater part of the cancer life-history; biopsy within 5 years is likely to reveal carcinoma *in situ*. The first two points may be conceded, but it is doubtful if the other two are invariably, or indeed often, true. It is noteworthy that in the series of 13 cases mentioned above (11 previous biopsy and 2 previous curettage) only 1 subsequent cancer was in Stage III and none in Stage IV; indeed, in 3 cases the later diagnosis was still of carcinoma *in situ*—at 2½, 4 and 6 years after the earlier specimen had been obtained. Since the subsequent cancers were, with only 1 exception, relatively localized, there is some reason to suspect that neoplasms with a protracted *in situ* phase are slow-growing throughout their entire evolution. Cancers which are already widespread when first seen may well undergo their whole development in a very short time, providing little opportunity for earlier diagnosis. This is also the view of Wespi (1952) who believes that only a minority of invasive cancers pass through a protracted intra-epithelial phase.

Another possibility to be considered is that invasion may already have been present at the time of the earlier examination. In many reported cases the diagnosis of intra-epithelial carcinoma was made from limited biopsy and curetted material; if the whole cervix had been available for study some signs of invasion might have been detected. For example, the case of Younge, Hertig and Armstrong (1949) which showed invasion 11 months after carcinoma *in situ* had been diagnosed is extremely suspect. This point is also illustrated by 2 cases encountered in Aberdeen; both patients were submitted to partial amputation of the cervix in the course of pelvic floor repair, and carcinoma *in situ* was discovered in the vicinity of the external os. The level of amputation seemed to be well above the abnormal epithelium and no further steps were taken. One woman returned one year, the

other two years later, both with Stage II cancer of the cervix.

Scipiades and Stevenson (1938) state that in some cases serial sections will reveal invasive activity although only carcinoma *in situ* is evident in the biopsy specimen. Martzloff (1944), Gusberg, Fish and Wang (1953) and Hoffman, Farell and Hahn (1954) have all described intra-epithelial carcinoma as a marginal phenomenon occurring in the vicinity of invasive cancer—an observation originally made by Schottländer and Kermauner in 1912. The transition from normal squamous epithelium through carcinoma *in situ* to invasive cancer is frequently seen in biopsy material; if the tissue is resected short of the invasive area an erroneous diagnosis of intra-epithelial carcinoma may easily be made. Conical resection of the cervix, including the entire squamo-columnar junction and the greater part of the canal, would appear to be the most satisfactory biopsy procedure. If serial sections indicate that the lesion is truly intra-epithelial, the method of resection may in itself prove adequate as a means of treatment. TeLinde and Galvin (1944), Anderson (1953) and other writers, however, favour total hysterectomy with removal of a liberal vaginal cuff, but this seems to be an unduly radical step unless other indications are present or evidence is forthcoming that carcinoma *in situ* as currently diagnosed invariably progresses to invasive and lethal malignancy. The small but not entirely negligible risk from hysterectomy might outweigh any reduction in subsequent cervical cancer mortality.

So many cases of intra-epithelial cancer are nowadays being reported that by their numbers alone suspicion is aroused that by no means all of them would progress to invasion if left untreated. Younge, Hertig and Armstrong (1949), for instance, reported 135 carcinomata *in situ* collected during the 32 years 1916-1947 at the Free Hospital for Women, Brookline, whereas the same authors (Hertig and Younge, 1952) found 150 cases during the subsequent 4 years, 1948–1951. Obviously the chance of finding carcinoma *in situ* depends on the efforts made to detect its presence, a point noted by Anderson (1953) in regard to his own experience in Edinburgh. He found 5 cases in 1948 (several blocks from each cervix sent to the laboratory), 8 in 1949 (ring blocks on all cervices submitted for histological examination), 23 in 1950 and 26 in 1951 (cervical smears and cervical curettage as screening methods, confirmed by biopsy).

Certain authors, including Pund and Auerbach (1946) and Younge, Hertig and their associates (1949, 1952), are definitely of the opinion that carcinoma *in situ*, if untreated, is a progressive lesion. Taylor (1952), on the other hand, believes that only 10 to 20 per cent of all lesions designated intra-epithelial cancer are destined to become invasive and lethal. He states that the incidence of invasive cervical cancer in New York State is 63 per annum per 100,000 females aged 40 years and over; assuming that carcinoma *in situ* could be detected at any single examination during the 5 years preceding the diagnosis of invasive cancer, then the maximum incidence of such lesions should be only 5 times that of overt cancer, namely 315 per 100,000 or 0·3 per cent. This estimate is in agreement with the actual experience of Wilcox, Pederson and Kischer (1956), who found 33 unsuspected cervical cancers among 9,815 women examined (0·34 per cent). Many clinics, however, report detection rates for carcinoma *in situ* considerably in excess of these figures. Auerbach and Pund (1945) found 2 cases in 100 cervices (2·0 per cent); Pund and Auerbach (1946), 47 in 1,200 cervices (3·9 per cent); Younge *et al.* (1949), 37 in 2,262 cervical specimens (1·64 per cent); Howard, Erickson and Stoddart (1951), 14 in 400 complete cervices (3·5 per cent); Gusberg (1951), 10 in 500 gynaecologically normal women (2·0 per cent); Carter *et al.* (1952), 126 in 18,632 gynaecological patients (0·67 per cent); and Reagan and Hicks (1953), 100 in 5,044 cervical specimens (2·0 per cent). In this country, Anderson *et al.* (1953) found entirely unsuspected cervical cancers, the majority intra-epithelial, in 1·1 per cent of a series of gynaecological patients. These data refer, of course, for the most part to gynaecological cases and it may be that the incidence of carcinoma *in situ* is correlated with the nature of the condition, investigation and treatment of which provided the specimen for examination. Nevertheless, the numbers are on the whole so much in excess of expectation that one may

suspect that by no means all of them would have become invasive if left untreated.

That errors in diagnosis occur is illustrated by the statement of Bechtold and Reicher (1952) that they have been confused by the appearances both cytological and histological produced by trichomonad infection. Novak and Galvin (1951) describe a series of 25 cases mistakenly diagnosed as intra-epithelial cancer due to technical faults in preparation of the sections and to misinterpretation of basal cell hyperplasia and metaplasia. But even when the usual criteria are fulfilled it would seem that histological examination cannot differentiate the progressive from the static, or perhaps even reversible, lesion.

In the present state of knowledge one tends to agree with McKelvey (1952) that the term "carcinoma *in situ*" or its equivalents should be avoided for the concept of such a lesion promotes the risk of incomplete therapy on the one hand and of unnecessary treatment on the other. The word "cancer" carries the implication that if not eradicated the lesion will eventually destroy the host, an attribute which almost certainly does not appertain to many cases designated "intra-epithelial carcinoma".

In order to clarify the situation there would appear to be two main lines of approach; firstly, a statistical evaluation of the whole problem of cervical cancer as it presents in any particular area, and secondly, intensive investigation into the biological characteristics of various epithelial abnormalities. A brief outline will be given of work on these lines which is now being undertaken in Aberdeen.

As already noted, 20 new cases of cervical cancer occur annually among the 52,000 married women resident in Aberdeen City. This provides a yardstick by which to measure the success of any campaign to detect and deal with intra-epithelial lesions and it also indicates the magnitude of the task involved. If *all* cervical cancers evolve over a period of 5 years, then at any given date 100 women in the City will already have developed carcinoma *in situ*; if a period of 10 years is accepted, this number becomes 200. These figures, 100 or 200 among 52,000 (1 in 520 or 1 in 260), represent the maximum likelihood of detecting *in situ* lesions in a representative sample of married women living in the City of Aberdeen. If, as seems more likely, some cancers evolve rapidly the chance of successful detection becomes correspondingly less. Since it is impossible to contemplate a screening programme on such a vast scale, an attempt has been made to discover the types of women most liable to develop cervical cancer, and this investigation will be reported in a later paper. It can be shown that women of high parity are particularly prone to the disease, not necessarily because of excessive childbearing but perhaps because as a rule they come from the lower income groups and tend to marry at a very early age. Since these women provide the reservoir from which a high proportion of cervical cancer cases is drawn, it is logical to concentrate diagnostic efforts on them. For some time all women aged 45 years and over who have had 4 or more pregnancies and who are admitted to the gynaecological wards for any reason at all have been submitted to careful clinical and cytological investigation of the cervix and in many instances to histological examination as well; it is proposed to extend this study to women without gynaecological symptoms referred by their own doctors to a special clinic. Details are not yet available but if it is true that intra-epithelial cancer is a progressive lesion and that invasive cancer is generally preceded by an *in situ* phase of significant duration then two points should emerge from this enquiry: (1) a higher than average rate of carcinoma *in situ* should be found and (2) as a result of treatment at the intra-epithelial stage the annual number of new cases of cervical cancer contributed by these women should fall in the years to come.

As regards the more direct study of intra-epithelial lesions, Antoine (1954) has suggested research on the lines of tissue culture experiments, investigation of cellular metabolism and enquiry into biophysical characteristics in order to substantiate the complete identity of certain epithelial lesions with invasive malignancy. An investigation is now being carried out in Aberdeen into the presence of the enzyme $\beta$-glucuronidase in the vaginal fluid. American workers, notably Fishman and his colleagues (Kasdon, Fishman and Homburger, 1950) and Odell and Burt (1950), have found that the

enzyme level is raised in pre-menopausal women with cervical cancer, and there is some suggestion that the level may also be elevated in certain *in situ* cases (Fishman *et al.*, 1954). It seems possible, therefore, that this test may prove of value in differentiating the significant intra-epithelial lesion from that which is of little consequence.

The best chance of progress is certainly to seek out women and to detect lesions which are confined to the epithelium but a sense of perspective must be maintained. Any screening programme should be planned in the light of past experience of invasive cancer and its success should be judged only by a reduction in incidence and mortality rates from the disease in the future.

## Conclusions

Cancer of the cervix probably exists in two main forms: one evolving rapidly, giving little opportunity for early diagnosis and highly lethal in its behaviour; the other slowly-progressive and relatively amenable to treatment. As regards the former variety, the minimum of delay between the onset of symptoms and the administration of treatment offers the best chance of survival to the individual patient but reduction in average delay would probably not contribute any striking improvement in overall survival rates, since even if treated at once the outlook for such cases is not good. The other type of case may have a protracted intra-epithelial phase and even after invasion occurs it tends to remain localized to the cervical region for a relatively long time. It is here that efforts at earlier diagnosis are likely to be most successful, but since in general these cases provide the successes of cancer therapy the influence of earlier detection on overall survival statistics may be less marked than expected.

In theory there can be no doubt that in all cases a better prognosis should be obtained if treatment is given as soon as possible, but it is unwise to adopt an unduly optimistic attitude. To induce patients with abnormal haemorrhage to report at once is not easy for it is natural that the woman should in the first instance regard her symptoms as transient and unimportant; once she does seek medical advice, thorough investigation should be the invariable rule but on the whole no significant advance should be expected from efforts directed towards the symptomatic phase of invasive cancer. The detection of lesions already invasive but producing no characteristic features is also unlikely to contribute any striking advantage. While the malignant nature of such cases is not in doubt, their numbers are small and the efforts needed to detect them out of proportion to the benefits likely to ensue. When any woman—and especially one regarded as particularly susceptible to the disease—consults a gynaecologist, the cervix should always be examined with care to exclude the presence of invasive cancer but specialized procedures such as routine cytology are probably not justified. It is in regard to intra-epithelial lesions that screening projects should prove most profitable but a critical approach is essential. In the first place, as already suggested, probably only a proportion of all cervical cancers undergo a prolonged *in situ* phase so that the statistical chance of successful detection is considerably less than might be thought; moreover, these cases are probably those most amenable to treatment at any stage in their development. One must also consider what proportion of all lesions currently regarded as intra-epithelial carcinoma are in fact potentially lethal; if some are static or reversible, their detection and eradication can have no influence on cancer statistics. Many hysterectomies may be performed and some women may die from the operation, and yet the incidence and mortality rates of cervical cancer remain unchanged.

Research is urgently required to discover methods to distinguish truly pre-invasive intra-epithelial lesions, which constitute probably only a minority of the total number of cases diagnosed histologically as carcinoma *in situ*. It would also be valuable if those centres which have accumulated a wide experience of carcinoma *in situ* would now correlate their results and conclusions with the overall picture of cervical cancer as it presents in the area concerned. Unless and until the incidence and mortality of the disease can be shown to have fallen, the value of much present-day work must be regarded as "not proven".

## References


Aitken-Swan, J., and Paterson, R. (1955): *Brit. med. J.*, **1**, 623.

Anderson, A. F. (1953): *J. Obstet. Gynaec. Brit. Emp.*, **60**, 353.

Anderson, A. F., Grant, M. P. S., McBryde, R. M., and Cockburn, M. K. (1953): *J. Obstet. Gynaec. Brit. Emp.*, **60**, 345.

Antoine, T. (1954): *Amer. J. Obstet. Gynec.*, **68**, 466.

Auerbach, S. H., and Pund, E. R. (1945): *Amer. J. Obstet. Gynec.*, **49**, 207.

Bechtold, E., and Reicher, N. B. (1952): *Cancer*, **5**, 442.

Carter, B., Cuyler, K., Thomas, W. L., Creadick, R., and Alter, R. (1952): *Amer. J. Obstet. Gynec.*, **64**, 833.

Donaldson, M. (1955): *Lancet*, **1**, 959.

Fishman, W. H., Green, S., Homburger, F., Kasdon, S. C., Neiburgs, H. E., McInnis, G., and Pund, E. R. (1954): *Cancer*, **7**, 729.

Galvin, G. A., Jones, H. W., and TeLinde, R. W. (1952): *J. Amer. med. Ass.*, **149**, 744.

Goldscheider, G., and Stern, B. E. (1955): *Brit. med. J.*, **2**, 1448.

Gusberg, S. B. (1951): *Amer. J. Obstet. Gynec.*, **61**, 276.

Gusberg, S. B., Fish, S. A., and Wang, Y. Y. (1953): *Obstet. Gynec.*, **2**, 557.

Hertig, A. T., and Younge, P. A. (1952): *Amer. J. Obstet. Gynec.*, **64**, 807.

Hoffman, J., Farell, D. M., and Hahn, G. A. (1954): in *Prophylaxis in gynecology and obstetrics (International Congress on Gynecology and Obstetrics, Geneva, 1954)*. Geneva: Librairie de l'Université, Georg et Cie., s.a., p. 152.

Howard, L., Erickson, C. C., and Stoddart, L. D. (1951): *Cancer*, **4**, 1210.

Kasdon, S. C., Fishman, W. H., and Homburger, F. (1950): *J. Amer. med. Ass.*, **144**, 892.

Lawson, J. G. (1956): *J. Obstet. Gynaec. Brit. Emp.*, **63**, 819.

McKelvey, J. L. (1952): *Amer. J. Obstet. Gynec.*, **64**, 816.

Martzloff, K. H. (1944): *Amer. J. Obstet. Gynec.*, **48**, 794 (discussion).

Novak, E. R., and Galvin, G. A. (1951): *Amer. J. Obstet. Gynec.*, **62**, 1079.

Odell, L. D., and Burt, J. C. (1950): *J. Amer. med. Ass.*, **142**, 226.

Pund, E. R., and Auerbach, S. H. (1946): *J. Amer. med. Ass.*, **131**, 960.

Reagan, J. W., and Hicks, D. J. (1953): *Cancer*, **6**, 1200.

Schottländer, J., and Kermauner, F. (1912): *Zur Kenntnis des Uteruskarzinoms. Monographische Studie über Morphologie, Entwicklung, Wachstum, nebst Beiträgen zur Klinik der Erkrankung*. S. Karger, Berlin.

Scipiades, E., and Stevenson, C. S. (1938): *Arch. Gynäk.*, **167**, 416.

Taylor, H. C. (1952): *Amer. J. Obstet. Gynec.*, **64**, 826 (discussion).

TeLinde, R. W., and Galvin, G. A. (1944): *Amer. J. Obstet. Gynec.*, **48**, 774.

Way, S. (1951): *Malignant disease of the female genital tract*. Churchill, London.

Wespi, H. J. (1952): *Gynaecologia, Basel*, **133**, 169.

Wilcox, H. R., Pederson, E. S., and Kischer, C. W. (1956): *Surg. Gynec. Obstet.*, **102**, 215.

Younge, P. A. (1939): *Arch. Path.*, **27**, 804.

Younge, P. A., Hertig, A. T., and Armstrong, D. (1949): *Amer. J. Obstet. Gynec.*, **58**, 867.

# CLEARANCE RATES OF RADIOSODIUM FROM MYOMETRIUM

BY

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## INTRODUCTION

A METHOD employing radiosodium for the experimental study of peripheral circulation was introduced by Kety (1948, 1949). He investigated the local clearance from a tissue of injected radioactive saline and considered the clearance rate as offering a "clinically useful means for the measurement of effective circulation in a particular tissue".

Many workers have since made use of this technique in measuring clearance rates from skeletal muscle in normal subjects and in the study of peripheral vascular disease. Clearance rates from subcutaneous tissues, from skin, from tubed skin pedicles and from the knee joint have all been measured and recently Morris, Osborn and Payling Wright (1955) have applied the method to the measurement of effective circulation of the uterine wall in late pregnancy.

Using a similar method we have carried out a survey of clearance rates from the myometrium in pregnancy and examined the effect of various factors, including the duration of pregnancy, age of patient, placental position, etc., on the clearance rates in both normal and toxaemic subjects.

## MATERIAL

Measurement of clearance rate was made or attempted in 112 consecutive cases between the 31st and 43rd weeks of pregnancy. Of these only 5 had to be discarded as failures because either a blood vessel was entered or an anomalous curve was obtained (i.e., the test was successfully carried out in more than 95 per cent of cases attempted). In 20 cases there were miscellaneous abnormal conditions present (cardiac disease, diabetes, twins, hydramnios) and these have not been included in the results reported here. There remain for analysis 87 patients (60 primigravid and 27 parous) of whom 40 were normal cases and 47 showed signs of pre-eclampsia. We have classified as pre-eclamptic any patient whose blood pressure exceeded 120/80 for the first time on at least two occasions in late pregnancy, recorded at rest, as an out-patient or in-patient. These cases were later subdivided according to different criteria of severity.

## METHODS

The test was carried out with the patient recumbent in her own bed. The nature and purpose of the procedure were explained and the patient's consent obtained.

After injecting local anaesthetic into the abdominal wall in the midline just above the umbilicus a 21 G gauge needle was introduced obliquely into the myometrium.

After a check aspiration for blood or liquor 0·4 ml. normal saline containing approximately 10 $\mu$c. $Na^{24}$ was injected. In 11 cases the volume injected was 1 ml. The clearance rates in these cases did not differ significantly from the remainder of the series. The skin was wiped clean, and a Geiger-Muller counter positioned over the injection site. The counter (G.E.C. type GM-4) was mounted in an aluminium holder and the end window screened with a 1·5 mm. thick brass cap. By trial movements of the counter the position of maximum count rate was rapidly located and the counter then

strapped in position with adhesive tape. The cable connecting the counter to a rate meter was passed through a ferrule on a bed cage placed over the abdomen and this helped to keep the G.M. tube in an upright position, despite the regular movements accompanying respiration and the frequent erratic movements of the foetus. Readings were taken at half-minute intervals on an Airmec Radiation Monitor (type 1021) and subsequently plotted against time on semilog paper. In almost all cases straight line graphs resulted, indicating that clearance was logarithmic, i.e., that the same fraction of the sodium present at any instant was removed per unit time. Sometimes irregularities were observed in the first minute or two after injection but more frequently the plot was linear from the onset.

The initial count rate was usually of the order of 300 cts./sec., but frequently higher and occasionally lower rates were observed, depending on the thickness of the abdominal wall, depth of injection, etc. The initial background (natural) was only 15 cts./min. The clearance was followed for some twenty minutes or until the count rate fell to 20–30 cts./sec. and then the test was concluded. The counter was then detached from the injection site and positioned first over the right-hand side and then over the left-hand side of the abdomen to take a "final background" reading on each side. This gave a measure of the active material present in the "counter-sensitive tissue" lying beneath the G.M. tube after diffusing from the injection site. This reading was almost always 10–12 cts./sec.

We did not find it necessary to employ the complex background correction described by Morris *et al.* (1955) as this correction is often negligible except in the terminal part of the curve, which can be ignored on most occasions when determining the half-time value. In a few cases, where the initial count rate was low and the clearance rate rapid, use was made of the "final background" measurement for correction. If the "final background" was (say) 10 cts./sec. after complete (or almost complete) clearance, then it must have been 5 cts./sec. after one "half-value time" from the start, 7·5 cts./sec. after two half-value times, and so on. These figures were easily subtracted graphically, no tedious calculations being necessary, and invariably a linear plot resulted.

There was, of course, no necessity to allow for the radioactive decay of $Na^{24}$ in such short-period experiments as these, nor was it necessary to allow for "lost counts" (due to finite resolving time of the apparatus) in the range of counts observed.

The radiation dose delivered in these experiments is very low. The total general body radiation due to 10 $\mu$c. $Na^{24}$ evenly distributed in a 70 kg. subject would amount during complete decay to only 0·016 equivalent röntgens even if none were excreted. The local tissue irradiation at the injection site is, of course, greater than this. It has been calculated (McGirr, 1952b) that the dose amounts to 0·5 e.r. per $\mu$c. injected—in our experiments about 5 e.r.—a value comparable with the skin dose in many diagnostic X-ray exposures.

We have chosen as an index of clearance rate the "half-value time" ($T\frac{1}{2}$) which is the time in minutes for the counting rate to fall by 50 per cent, and we refer to this simply as "the clearance time". We feel that this is simpler than the clearance constant (k) of Kety, or the circulation index (I) of Barron, Veall and Arnott (1951) but, for comparison of our results with those of other workers on different tissues it may be noted here that

$$k = \frac{0{\cdot}693}{T\frac{1}{2}\,(\text{min.})} \quad \text{and} \quad I = \frac{1{,}000}{T\frac{1}{2}\,(\text{min.})}.$$

McInally *et al.* (1952) make use of the "percentage clearance per minute" which is equal to 100 k.

## Results

A fairly wide range of clearance times was found even in normal subjects. Walder (1953, 1955) showed that in voluntary muscle during an *individual experiment*, either in human or controlled animal experiments, the changes in clearance rate are directly proportional to changes in blood flow, but that different clearance rates observed in *different subjects*, or even in repeat observations in the same subject, do not indicate proportionately different blood flows. The anatomical factors—the area of the capillary bed available for diffusion, proximity

of the injected depot to large blood vessels—will differ from one case to another. In all published work on skeletal muscle a wide scatter is reported for the clearance rates in the resting state; for example, McGirr (1952a) found repeat clearance rates in the same normal limb to vary by over 80 per cent, and those of right leg and left leg to differ by as much as 100 per cent of the lesser value.

It was, therefore, of primary importance to establish whether or not different myometrial clearance rates observed in different patients were of any significance, or whether repeated tests on the same patient at slightly different injection sites, might not reveal just as variable results as those found in different patients. With this in mind we carried out several duplicate and a few triplicate tests on the same patients. There was usually an interval of one week between these repeat tests, and an injection site close to but not identical with the previous one was used. The results observed in these patients are set out in Table I.

TABLE I
*Repeat Clearance Times on Same Patient*

| No. of Patient | Clearance Time in Minutes | | |
|---|---|---|---|
| | 1st Observation | 2nd Observation | 3rd Observation |
| 1 .. | 4·5 | 4·5 | — |
| 2 .. | 3·25 | 4·0 | — |
| 3 .. | 11·5 | 11·5 | — |
| 4 .. | 5·0 | 5·0 | 5·0 |
| 5 .. | 3·5 | 4·75 | — |
| 6 .. | 2·5 | 4·0 | 2·75 |
| 7 .. | 5·0 | 4·0 | 7·5 |
| 8 .. | 5·0 | 7·25 | — |
| 9 .. | 4·0 | 7·5 | — |
| 10 .. | 5·25 | 13·0 | — |

An analysis of variance among these results (Table II), in contrast to those reported on skeletal muscle, shows clearly that, despite the variability, the method is valid for detecting real differences in clearance rate between different subjects.

The results for all normal and all pre-eclamptic patients are set out in Table III, which takes no account of parity or any other factors. In this and subsequent tables the number of cases (N) in each group is shown, and the mean value of the clearance time for the group, with the standard error of the mean. In the right-hand column is given the probability (P) that the difference between the means of two groups could be expected to occur merely by chance.

TABLE II
*Analysis of Variance*

| Source of Variation | Sum of Squares | Degrees of Freedom | Variance Estimate |
|---|---|---|---|
| Between-Patient .. | 129·66 | 9 | 14·407 |
| Within-Patient .. | 47·54 | 13 | 3·65 |
| | 177·20 | 22 | |

$$F = \frac{14 \cdot 41}{3 \cdot 65} = 3 \cdot 95 \quad \cdot 05 > P > \cdot 01.$$

TABLE III

| | N | Mean $T\frac{1}{2}$ (minutes) | Students t |
|---|---|---|---|
| All normal pregnancies .. | 40 | 6·54 ± ·558 | ·05 > P > ·02 |
| All pre-eclamptic pregnancies .. | 47 | 8·32 ± ·578 | |

It will be seen that cases of pre-eclampsia give significantly slower mean clearance times than do normal cases, as was demonstrated by Morris *et al.* (1955, 1956). The mean clearance time, derived from their series, for all cases of pre-eclampsia as defined in this paper is 8·5 minutes. On breaking down the data into smaller but more homogeneous groups other interesting differences are apparent. In the remaining tables a separation of primigravid from parous patients has been made, since in several respects the two groups differ.

### INFLUENCE OF DURATION OF PREGNANCY

In Table IV the cases in each group are divided into those who were past term and those who had not reached term. The effect of prolongation of pregnancy on the clearance time is very clearly demonstrated in both normal and pre-eclamptic patients, particularly amongst primigravidae.

TABLE IV
*Influence of Maturity in Normal and Pre-eclamptic Pregnancies*

| | | N | Mean $T\frac{1}{2}$ (minutes) | Students t |
|---|---|---|---|---|
| Primigravidae: | | | | |
| Normal: | Before Term .. .. | 14 | 5·07± ·452 | ·01>P>·001 |
| | After Term .. .. | 12 | 8·10±1·145 | |
| Pre-eclamptic: | Before Term .. .. | 25 | 7·14± ·76 | ·001>P |
| | After Term .. .. | 9 | 13·58± ·479 | |
| Multigravidae: | | | | |
| Normal: | Before Term .. .. | 12 | 6·21±1·18 | |
| | After Term .. .. | 2 | 9·5 | |
| Pre-eclamptic: | Before Term .. .. | 8 | 6·7 ± ·469 | Difference not significant |
| | After Term .. .. | 5 | 7·2 ±1·139 | |

TABLE V

| | | N | Mean $T\frac{1}{2}$ (minutes) | Students t |
|---|---|---|---|---|
| Primigravidae: | | | | |
| Before Term: | Normal .. .. | 14 | 5·07± ·452 | ·1>P>·05 |
| | Pre-eclamptic .. | 25 | 7·14± ·760 | |
| After Term: | Normal .. .. | 12 | 8·10±1·145 | ·01>P>·001 |
| | Pre-eclamptic .. | 9 | 13·58± ·479 | |

### INFLUENCE OF PRE-ECLAMPSIA

From the data in Table V the effect of pre-eclampsia is seen more clearly than from the pooled data given in the earlier table.

It will be noted that the slowing of the clearance rate associated with pre-eclampsia in primigravidae is aggravated when pregnancy is prolonged, the slowing effects being additive. The contrast between the clearance times before term in normal cases, and after term in pre-eclamptics is shown graphically in Figure 1 where two individual results typical of these groups are reproduced.

The differences between these subgroups amongst the parous patients are not significant. This is discussed later.

Up to this point we have grouped together all the cases of pre-eclampsia. Because of the difficulty of classifying the severity of the condition by any single criterion, we later subdivided the whole group in a number of ways according to several different criteria. No significant correlation with either the height of the blood pressure or the degree of albuminuria was obtained. Morris *et al.* (1956) found a correlation between diastolic blood pressure and clearance time. The difference of results may well be due to the fact that there was a preponderance of mild cases of pre-eclampsia in the present series.

The influence of the duration of signs and symptoms prior to the test in those cases of pre-eclampsia without albuminuria is shown in Table VI.

TABLE VI
*Pre-eclampsia Without Albuminuria*
*Influence of Duration of Pre-eclampsia*

| Duration of Illness | N | Mean $T\frac{1}{2}$ (minutes) |
|---|---|---|
| 1 week .. .. | 6 | 7·60±1·148 |
| 2–3 weeks .. .. | 4 | 8·25±2·165 |
| 4 weeks .. .. | 10 | 11·38±1·920 |

It will be seen that as the duration of the condition increases, so the mean clearance rate becomes slower. However, the t test for significance between the means of the one week and the four week groups indicates that 0·2>P>0·1

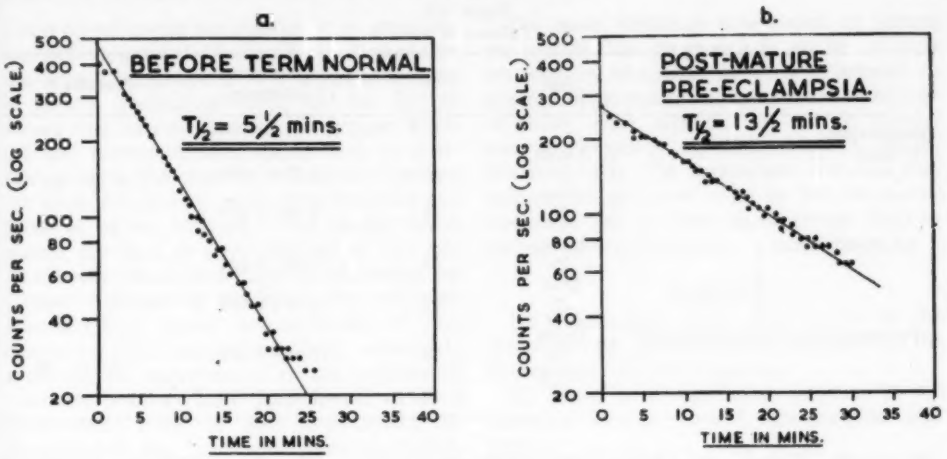


FIG. 1

Two typical graphs showing (*a*) rapid clearance in a normal patient before term, and (*b*) slow clearance in a post-mature case of pre-eclampsia.

so that statistical significance cannot be claimed for the observed difference. However, we consider the trend is a real one, since only the more mild cases were treated conservatively for several weeks. This trend was not found among the cases of pre-eclampsia with albuminuria, possibly because the progress of the condition is often more abrupt in such cases, and because of the selection of cases above mentioned.

### INFLUENCE OF PARITY

Comparing the results for normal primigravidae with those for normal parous patients no effect can be seen which could be specifically attributed to parity. The difference between the means is not significant.

It is noteworthy that, whereas among the primigravidae pre-eclampsia is associated with a slower clearance time, among the parous women this difference is not found. However, the pre-eclampsia in these parous cases was of milder type (only one showed albuminuria) and the mean age of these patients was, of course, greater than that of the primigravidae. The relevance of this fact is discussed below. There is also evidence (Horn, 1917) that the blood vessels of the parous uterus are larger and more abundant.

### INFLUENCE OF AGE

In Table VII the data is set out dividing the cases in each group into those younger than 25 years and those who were 25 or older. The reason that this age was chosen as the dividing line was that it gave groups of most nearly comparable size.

The most striking fact that emerges from this analysis is that, whereas amongst normal primigravidae the older women have a slower mean clearance time, among patients suffering from pre-eclampsia, it is the younger women who have the slower clearance times. This would appear to be in accord with the clinical observation that pre-eclampsia occurs in a more severe form in young women.

It is relevant to compare this effect of age in pre-eclampsia with the findings of Nelson (1955) in a statistical study of pre-eclampsia. He noted that the incidence of mild pre-eclampsia (based on the criteria of elevated B.P. alone) rises sharply after the age of 30 and comments: "Since this is also the age at which essential hypertension begins to show itself to any extent in women (Robinson and Brucer, 1939) the question arises as to whether the rise is due to true mild pre-eclampsia or whether pregnancy

TABLE VII
*Influence of Age*

| | Age | N | Mean $T\frac{1}{2}$ (minutes) | Students t |
|---|---|---|---|---|
| Primigravidae: | | | | |
| Normal .. .. .. .. | Under 25 | 11 | 5·20± ·455 | 0·1>P>·05 |
| | Over 25 | 15 | 7·40±1·017 | |
| All pre-eclamptics .. .. | Under 25 | 22 | 10·06±1·104 | 0·1>P>·05 |
| | Over 25 | 12 | 6·71±1·059 | |
| Pre-eclamptics without albuminuria | Under 25 | 10 | 11·98±1·686 | ·05>P>·02 |
| | Over 25 | 10 | 7·35±1·170 | |

has simply 'brought out' latent hypertensive tendencies."

It is likely, therefore, that our older patients include many "latent essential hypertensives" whereas the younger group would presumably consist mainly of true pre-eclamptics and few, if any, essential hypertensives. This may well be the reason why the clearance times are longer in the younger women with pre-eclampsia.

### Influence of Placental Location

In 15 cases the placenta was localized by radiography. The clearance times for those having an anterior placenta have been compared with those where the placenta was not anterior, the two groups being of similar composition in other respects.

TABLE VIII

| | N | Mean $T\frac{1}{2}$ (minutes) | Students t |
|---|---|---|---|
| Anterior placenta .. | 7 | 8·25±1·249 | 0·05>P>0·02 |
| Non-anterior placenta .. | 8 | 4·75± ·739 | |

The mean value for the clearance time is considerably slower in those cases having an anterior placenta and the difference between the means of the two groups is significant. The explanation for this somewhat unexpected result is not clear.

### Influence of Other Factors

The data has also been analyzed to see if either placental weight, infant's birth weight or duration of rest in bed could be correlated with the observed clearance times, but no such correlation was found to exist.

### Discussion

The most significant observation in this series of tests is the reduced myometrial clearance rate that is found when normal pregnancy is prolonged. This reduction is even more marked in cases of pre-eclampsia. Both in the normal and the pre-eclamptic groups, the difference between the mean rates before and after term is highly significant ($P<·01$).

The clearance rate in postmature normal primigravidae is comparable with that in pre-eclamptics before term, the respective mean half-times for these groups being 8·1 and 7·1 minutes. If, however, pregnancy complicated by pre-eclampsia continues past term, the mean clearance rate is halved, the harmful effects being cumulative. There is undoubtedly a double danger in allowing cases of pre-eclampsia to continue past term. These findings may be compared with those of Walker and Turnbull (1953) and Mackay (1955). The former workers showed that, as pregnancy is prolonged, the

foetal blood leaving the placenta is progressively less well oxygenated. Mackay has confirmed that the oxygen saturation of cord blood is reduced in normal postmature cases, and has further shown that in pre-eclampsia the oxygen levels are still further reduced, particularly in postmature cases. The remarkable congruity between the present results on myometrial clearance and those of others on cord blood oxygen levels should not lead to over-emphasis of the role that uterine blood flow plays in influencing the uptake of oxygen by the foetus. For, although Morris (1955) found that treatment of pre-eclampsia with hypotensive drugs commonly produced an improvement in the myometrial clearance rate, we have seen several cases of intra-uterine death in such cases where the hypertension has been adequately controlled, and Morris also refers to this danger. In such cases irreversible morbid changes in the placenta must have taken place, and little is achieved by hypotensive drug therapy.

The results obtained in pre-eclampsia show the same trend as those of Morris *et al.* (1955, 1956). Although they reported in the earlier paper a mean clearance time of 15·3 min. in 8 cases of severe pre-eclampsia, in the 6 such cases subsequently added to this group the mean clearance time was only 8·8 min., which is similar to our mean figure for all cases of pre-eclampsia (8·3 min.). The degree of reduction in the "effective circulation" in the myometrium in pre-eclampsia is probably more nearly two-fold than fourfold. This is, of course, a comparison of the average results, and there is considerable variation within the groups of cases.

The site of injection was also different from that used by Morris *et al.* We chose the midline above the umbilicus because it was an area distant from the main vascular trunks and branches to the myometrium where a more homogeneous and representative area of capillary bed might be found. It was thought that injections a few centimetres below the umbilicus would not necessarily avoid the placental site, as they would still be well within the upper segment. The slower clearance times found in cases with an anterior placenta are not readily explained.

The mean clearance time found in normal patients in late pregnancy is similar to that reported by Morris *et al.* It is of interest to compare these results on plain muscle with those of many other workers on resting skeletal muscle (Cooper *et al.*, 1949; McGirr, 1952b; Walder, 1953). The comparison indicates that myometrial clearance rates in late pregnancy are some two or three times greater than in resting voluntary muscle.

## Summary

(1) Observations have been made of the clearance rate of radiosodium injected into the myometrium in late pregnancy.

(2) There is a significant slowing of the clearance rate in normal primigravidae past term.

(3) There is a significant slowing of the clearance rate in pre-eclampsia. In cases of pre-eclampsia which are also past term, there is an even more marked reduction in clearance rate.

(4) In pre-eclampsia, clearance rates among younger women are slower than among older women. This is thought to be due to the inclusion of benign latent hypertensives in the latter group. The reverse is found in normal pregnancy.

Among parous women the above differences are not clearly demonstrated, though the numbers of cases in the subgroups are small.

(5) No correlation was found between clearance rates and the degree of hypertension or of albuminuria in pre-eclampsia, nor with placental weight or infants' birth weight in any group of cases.

(6) The range of myometrial clearance rates observed, even in normal subjects, is quite large. This certainly limits the diagnostic value of the procedure, though results are reasonably reproducible in a single patient on separate occasions. But it is during a single test that changes in clearance rate most accurately reflect changes in blood flow. We are attempting to use this method to study the effects of drugs on myometrial blood flow.

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## References

Barron, J. N., Veall, N., and Arnott, D. G. (1951): *Brit. J. plast. Surg.*, **4**, 16.

Cooper, F. W., jr., Elkin, D. C., Shea, P. C., jr., and Dennis, E. W. (1949): *Surg. Gynec. Obstet.*, **88**, 711.

Horn, O. (1917): *Histologische Studien über den menschlichen Uterus*. Karger, Berlin.

Kety, S. S. (1948): *Amer. J. med. Sci.*, **215**, 352.

Kety, S. S. (1949): *Amer. Heart J.*, **38**, 321.

McGirr, E. M. (1952a): *Clin. Sci.*, **11**, 91.

McGirr, E. M. (1952b): *Brit. med. Bull.*, **8**, 192.

McInally, M., Campbell, J. A., Robertson, D. J., and Douglas, D. M. (1952): *Clin. Sci.*, **11**, 183.

Mackay, R. B. (1955): *Studies on the oxygenation of the foetus in normal and abnormal pregnancy*. M.D. Thesis, University of Edinburgh.

Morris, N. (1955): *J. Obstet. Gynaec. Brit. Emp.*, **62**, 696.

Morris, N., Osborn, S. B., and Wright, H. P. (1955): *Lancet*, **1**, 323.

Morris, N., Osborn, S. B., Wright, H. P., and Hart, A. (1956): *Lancet*, **2**, 481.

Nelson, T. R. (1955): *J. Obstet. Gynaec. Brit. Emp.*, **62**, 48, 58.

Robinson, S. C., and Brucer, M. (1939): *Arch. intern. Med.*, **64**, 409.

Walder, D. N. (1953): *Clin. Sci.*, **12**, 153.

Walder, D. N. (1955): *Clin. Sci.*, **14**, 303.

Walker, J., and Turnbull, E. P. N. (1953): *Lancet*, **2**, 312.

# FURTHER EXPERIENCE WITH HYPOFIBRINOGENAEMIA OF PREGNANCY

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AN opportunity presented in our unit to attempt further clarification of the pathological factors causing incoagulability of the blood in some cases of premature detachment of the placenta, and further to evaluate the role of early Caesarean section.

In the first case we reported we carried out Caesarean section within an hour of the admission of the patient because of over-riding obstetric necessity. At that time facilities for obtaining adequate emergency supplies of fibrinogen were not very advanced, and the operation was successfully completed before the fibrinogen became available. The patient made a rapid recovery from the shocked condition and replenished her own fibrinogen (without parenteral administration on our part) very soon after the uterus had been evacuated (Larkin and Philipp, 1956).

In the present case, which came our way after an interval of almost exactly two years, we were able to take advantage of the great improvement in the availability of fibrinogen, and from the obstetric aspect we had more latitude in choosing our moment to operate.

## CASE HISTORY

Mrs. Q., age 32.

*Previous Obstetric History*

1947—36 weeks, normal delivery of a male child weighing 4¼ pounds. Breast fed. Alive and well.

1948—38 weeks. Delivery of a stillborn child following toxaemia which developed at the 30th week. Before the delivery there was a concealed ante-partum haemorrhage. Blood transfusion was required.

1949—Full-time, normal delivery of female child weighing 8½ pounds. Breast fed. Alive and well.

1951—Full-time, normal delivery of male child weighing 8 pounds. Breast fed. Alive and well.

1952—Full-time, normal delivery of female child weighing 6½ pounds. Breast fed. Alive and well.

1954—42 weeks. Admitted to hospital having had an ante-partum haemorrhage with passage of "clots" at home. Already in labour. Blood pressure 140/90. Diagnosis of marginal placenta praevia was made. After six hours, normal delivery of live male child, 8¼ pounds, with minimal blood loss at and after delivery. Breast fed. Alive and well.

During the pregnancy which is the occasion of this report she attended her own doctor at monthly intervals. She was not referred for any specialist opinion. The L.M.P. was on 23rd March, 1956 and the expected date of delivery 30th December. Her blood pressure and everything else throughout was reported as "normal". Although she said she was pale throughout no investigations were undertaken.

On 30th November, 1956 she went to bed as usual at 11 p.m., but was kept awake by the baby kicking unusually violently. She slept fitfully, and at 2.30 a.m. on 1st December, 1956, after experiencing severe "wind" pains, she vomited bile. She returned to bed. The pains became worse, and at 5.30 a.m. she had a "very intense wind pain". She got out of bed to be sick, but collapsed on the landing and found that she was bleeding heavily. She had a sensation that something needed to come away. Her husband called the doctor. Foetal movements ceased at 6 a.m. The doctor arrived about half an hour

later, and without sedation she was sent to Oldchurch Hospital which she reached in a very shocked state at about 8 a.m.

The blood pressure was 90/50 mm. Hg. The pulse was weak at a rate of about 90. Pallor was extreme, and the patient was much distressed with upper abdominal pain. The uterus was hard and tender, especially on the right side. The vertex was felt just at the brim of the pelvis. By catheterization the bladder was found to be empty.

A diagnosis of concealed and revealed antepartum haemorrhage with anuria was made. Morphia gr. ¼ was given intramuscularly. Blood was taken for cross-matching, and an intravenous plasmosan infusion started at 8.15 a.m. When the laboratory technician on duty examined the specimen he saw a small clot but this disappeared again after 10 minutes, and the blood thereafter remained fluid. No clot formed after the addition of a knife-point of thrombin, though the potency of the thrombin sample was demonstrated in normal oxalated plasma. At 9.0 a.m. we took a further specimen into Wintrobe's oxalate mixture. On addition of thrombin to this some wispy threads of fibrin appeared. The fibrinogen level in the plasma from this specimen was later estimated by the micro-Kjeldahl method and found to be 33 mg. per cent.

At 9.0 a.m. a blood transfusion was started through a needle in the right arm, and at 9.30 a.m. a second transfusion was commenced with blood into the left arm. Neither transfusion would run very quickly owing to venous spasm, but the patient's condition had not further deteriorated.

At about this time vaginal examination was made. The cervix was found to be 2-fingers dilated but thick. The vertex was presenting, the head being only moderately flexed and not engaged. The membranes were ruptured, and about 2 pints of liquor flowed causing the patient quite considerable relief of her abdominal pain.

At 10 a.m. a further specimen of blood was taken which formed no clot whatever at any time.

At 10.30 a.m. a clot of blood was passed vaginally. No fibrinogen had at this stage been administered.

At 10.30 a.m. 20 ml. of blood was taken for the specific purpose of attempting to demonstrate a fibrinolysin, as related later. It was spun down at once, and after about 10 minutes a soft gelatinous thrombus formed in the plasma. Over the course of the next 4 hours, probably partly by contraction and partly by fibrinolysis, the thrombus reduced down to the size of a pea, and this residue remained stable for 24 hours.

Soon after 10.30 a.m. further sudden abdominal pain was experienced. The uterus was seen to be enlarging, more fluid blood was lost and the patient's condition temporarily deteriorated.

At 11 a.m. a further vaginal examination revealed that the cervix was possibly a little thinner, but the dilatation was not much greater than two fingers. The head seemed to be somewhat more deflexed, yet well applied to the cervix. There was fluid blood, but no clot in the vagina.

By mid-day a further vaginal examination revealed no progress. The head was now thought to have extended to a brow presentation. The explanation for this finding was puzzling indeed. The patient had by now received 3 pints of blood. Her blood pressure was 86/50 mm. Hg. The patient told us we were "getting nowhere". It was in fact clear that there was no prospect that she would deliver herself spontaneously within a reasonably short time, and it was felt that, if the clotting mechanism could be restored to normal, this would be the ideal time for surgical intervention.

Having learnt by previous experience that venous spasm can be very troublesome in this condition, almost bringing the transfusions to a standstill, the two blood transfusions were kept running into both arms, and a further "cut-down" was made into the left ankle. Fibrinogen, 1·8 g., was administered with quite remarkable improvement in the patient's condition. A specimen of venous blood was taken from the right foot 10 minutes after the fibrinogen had been administered. This produced a thoroughly reassuring firm solid clot in 4 minutes. It remained stable up to the time of commencement of the operation but when re-examined some hours later was found to have dissolved. Our reasons for believing that administration

of this amount of fibrinogen may reasonably be effective are explained in our previous communication (Larkin and Philipp, 1956).

The patient was no longer obviously shocked, and was smiling and talking relatively happily when, at 12.45 p.m., she was anaesthetized by Dr. Thomas for Caesarean section.

It is regretted that a specimen for fibrinogen estimation was not taken at this time, but, as she had transfusions running into three limbs and was being prepared for operation, there was a certain amount of practical difficulty about obtaining blood, and the opportunity was missed.

Through a midline incision the abdomen was opened, and a little free blood was found in the peritoneal cavity. To our surprise the uterus did not appear to be "Couvelaire". A transverse incision in the lower segment of the usual length proved to be inadequate to deliver the extended head which could not be flexed, so Wrigley's forceps were applied gently, and at the edges the incision was elliptically extended to avoid the big vessels. The cord was not pulsating nor the foetal heart beating, but the anaesthetist was so impressed with the baby's fine muscle tone that he asked permission to inject adrenaline into his heart. He then realized that the child was in rigor mortis, and it was then clear that it was this condition that had caused the progressing hyperextension of the head.

Meanwhile the placenta was delivered. It had been four-fifths detached. Thirty ounces of clotted blood was removed from the uterus. This massive clot must obviously have formed before fibrinogen disappeared from the circulating blood, once again demonstrating that the placental detachment precedes the hypofibrinogenaemia.

The incision in the uterus was repaired in two layers. It was a quarter of an hour after starting the operation that troublesome bleeding first commenced from the left edge of the incision. Two or three mattress sutures were inserted, and a further 1·8 g. of fibrinogen was administered. Following this there was rapid improvement. A small "oxycel" pack was left before closing the utero-vesical peritoneum under which an empty corrugated drain was placed to extrude from the lower end of the abdominal wound to prevent intra- or retro-peritoneal blood collection.

The abdomen was closed in layers. At 1.30 p.m. the patient was conscious and fit enough to be moved off the soaked sheets on the operating table. A specimen of venous blood formed a firm solid clot which remained stable.

By 2.45 p.m. the blood pressure had risen to 100/60 mm. Hg, and the pulse, although at 112 per minute, felt stronger. By 4.30 p.m. the systolic pressure had risen to 120, but the diastolic pressure could not be recorded accurately.

At 9.30 p.m. the blood pressure was 140/95 mm. Hg. All transfusions were stopped, although the patient was still pale. A total of 7 pints of blood and 1 pint of "plasmosan" together with two bottles of reconstituted fibrinogen had been administered, but still no urine had reached the bladder. The total blood loss had probably exceeded 10 pints.

By the next morning the patient was fair in condition, and 10 ounces of urine was passed by catheter.

On 3rd December, 1956 the haemoglobin was 56 per cent, and the plasma fibrinogen was 466 mg./100 ml. The temperature was 102° F. The blood urea was 50 mg. per cent.

It was feared that early paralytic ileus was developing, but no gross distension occurred, and with only the administration of "Bepanthen", one ampoule three times in the next twenty-four hours and an enema, this danger passed, and so did flatus in quantity.

On 5th December, 1956 signs of consolidation at the base of the right lung appeared.

By 9th December, 1956 the patient appeared well and the stitches were removed. She was on "Inferon" therapy, although already by 6th December her haemoglobin had reached 66 per cent.

## Epilogue

One of the puzzles of this condition has been the part played by fibrinolysis. Numerous authors have reported formation and subsequent disappearance of clots, but have been unable to demonstrate lysis of exogenous preformed fibrin. In our previous case, some blood samples taken from the patient formed clots which disappeared in a few minutes. Yet when a very

small normal exogenous blood clot was incubated in the patient's plasma for 24 hours it did not undergo the slightest macroscopic change. The clues to this apparent anomaly are contained in three papers. Firstly, Mole (1948), in discussing the cadaveric fibrinolysin demonstrated in cases of sudden death, states that lysin added to blood or plasma after a thrombus has formed is not effective. Lytic activity is shown only if the lysin is present while the thrombus is actually forming.

Secondly, Macfarlane and Biggs (1948), writing in *Blood* on fibrinolysis in post-operative patients, state that, though preformed fibrin may slowly be digested, activity is greatly increased if the enzyme is present during the process of coagulation.

Thirdly, though the cadaveric fibrinolysin is relatively stable, the one investigated by Macfarlane and Biggs is not so. For this reason Fearnley, Revill and Tweed (1952) recommend that tests should be carried out as soon as possible after the blood is shed.

Accordingly, the following experiments were carried out on our patient's plasma immediately after the 10 o'clock specimen was withdrawn.

*Experiment 1.* Doubling dilutions of 1 ml. of normal citrated plasma were made down to a dilution of 1/128. Half a ml. of 2·5 per cent calcium chloride was added to each tube. After incubation for 20 minutes coagulation had occurred, and this took the form of a fine fibrin web in the higher dilutions. One ml. of the patient's plasma was added to each tube. After 4 hours there was no demonstrable fibrinolysis even in the highest dilutions.

*Experiment 2.* Doubling dilutions of 1 ml. of normal citrated plasma were made in two rows of tubes. To the back row ½ ml. calcium chloride and 1 ml. of saline were added. To the front row ½ ml. calcium chloride was added, and immediately afterwards, before coagulation had occurred, 1 ml. of patient's plasma was added to each tube. After incubation for 20 minutes, fibrin webs formed in the back row of tubes to a dilution of 1/128. In the front row, to which the patient's plasma had been added, fibrin webs formed to a dilution of 1/16 only. Furthermore, all the fibrin thrombi in the front row of tubes were much smaller than those in the back row. After 4 hours incubation there was considerable disparity in the size of thrombi in tubes at equivalent dilutions in the two rows. The second experiment was repeated after 48 hours with negative results.

We feel that these findings indicate the presence of a fibrinolysin of the type described by Macfarlane and Biggs, for which they accept the name "Plasmin".

## Conclusions

As a result of our survey of the experiences and opinions of others and of our own observations, we have tentatively formulated the following hypothesis.

In some cases of abruptio placentae (and in certain other obstetric conditions) thromboplastin is injected into the maternal circulation (Schneider, 1950). As a result intravascular fibrin is formed. At the same time, as the result of the shock, an active fibrinolysin is released which becomes adsorbed on to the intravascular fibrin as the latter is in process of formation and destroys it. In this way large quantities of fibrin are continuously formed and destroyed in the circulating blood.

Owing to the shock and the generalized vascular spasm (it is thought that hypersensitivity to foreign protein from the placental site may play a part in this) the blood supply to the liver is reduced. As long as this situation obtains the liver does not replenish fibrinogen to the circulation, though in its normal state it is capable of doing so quite rapidly. Incidentally, reduction of the blood supply to the kidneys, because of the generalized vascular spasm, at the same time usually produces anuria as in this case, and in extreme cases renal cortical necrosis (Sheehan and Moore, 1952).

A vicious circle is thus set up in which the blood becomes incoagulable and will remain so, so long as the patient is shocked. As long as the blood is incoagulable the patient will go on bleeding. The more the bleeding the deeper the shock.

In order to break this vicious circle it is necessary to combat shock and to empty the uterus. The condition of shock should not be allowed to continue long enough to endanger the kidneys. If natural labour is not progressing

fairly rapidly, Caesarean section should be resorted to, covered by parenteral administration of fibrinogen.

Then the fibrinolysin, which has a limited stability, will disappear from the blood, and will not return so long as the state of shock has been successfully and permanently overcome.

## References


Fearnley, G. R., Revill, R., and Tweed, J. M. (1952): *Clin. Sci.*, **11**, 309.

Larkin, I. M., and Philipp, E. E. (1956): *J. Obstet. Gynaec. Brit. Emp.*, **63**, 422.

Macfarlane, R. G., and Biggs, R. (1948): *Blood*, **3**, 1167.

Mole, R. H. (1948): *J. Path. Bact.*, **60**, 413.

Schneider, C. L. (1950): in *Ciba Foundation Symposium: toxaemias of pregnancy, human and veterinary*. Churchill, London.

Sheehan, H. L., and Moore, H. C. (1952): *Renal cortical necrosis and the kidney of concealed accidental haemorrhage*. Blackwell Scientific Publications, Oxford.

# HYPOFIBRINOGENAEMIA WITH A 19-WEEKS ABORTION

BY

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A HAEMORRHAGIC diathesis due to hypofibrinogenaemia has been increasingly observed during the last few years following various obstetrical conditions, especially premature separation of the placenta, retention of a dead foetus *in utero* and amniotic fluid embolism.

A review of the literature shows that most of the cases have occurred during the final trimester, the shortest period of gestation being reported by Veprovsky and Levin (1956) when a macerated foetus was delivered by hysterotomy at the 22nd week. The case presented in this report occurred at the 19th week of pregnancy and the foetus was alive until a few hours before vaginal delivery.

## CASE REPORT

Mrs. D. B. first attended Saint Mary's Hospitals, Manchester, during her 8th pregnancy on 6th March, 1956. Her 7 previous pregnancies had all been uneventful and had each terminated in normal delivery at full-time of healthy babies ranging in weight from 6 pounds to 8 pounds. No relevant details were found in the previous medical or surgical history.

She was well on general examination. The last menstrual period had occurred on 23rd December, 1955 and the uterus was enlarged to a size consistent with the 10-weeks amenorrhoea. Analysis of the urine was normal and her blood pressure was 115/70. Routine examination of the patient's blood showed it to be Group O Rhesus Positive; the Wassermann reaction and Kahn test were both negative, and the haemoglobin estimation was 75 per cent (11·1 g.).

In view of her grand multiparity she was booked for confinement in hospital and asked to return to the clinic in 1 month's time. This appointment she failed to keep.

On 9th May, 1956, when 19½-weeks pregnant, she was admitted to the gynaecological ward as an emergency at 1 a.m.

She had remained well since her attendance at the clinic until 5 hours before admission, when heavy vaginal bleeding had started, followed half an hour later by severe labour-like pains. Foetal movements had been felt for the previous 3 weeks, but had disappeared during the preceding hour or so.

The blood pressure was 125/80 with a good pulse of 100 beats per minute, whilst the temperature was 98·0° F. Abdominal examination found the uterus to be larger than expected, reaching 2-fingers breadth above the umbilicus. It was tense and rather tender but undergoing contractions. Very little blood was oozing from the vagina at this time. She was considered to have an inevitable abortion and was given an analgesic.

The following morning her condition was satisfactory. However, in the afternoon the condition deteriorated rapidly, and at 2 p.m. she was shocked, with a blood pressure of 65/40 and a weak pulse of 140 beats per minute. It was now noted that the trickle of blood issuing from the vagina was not clotting. Blood was taken and an immediate transfusion of Dextran started together with routine anti-shock therapy. This blood sent to the laboratory did not clot and was later reported as having a fibrinogen level of only 68 mg. per cent, and a haemoglobin level of 52 per cent (7·7 g.).

Abdominal examination showed little change from that previously noted, though the uterus was now contracting and relaxing only very poorly. It was still tense, tender and larger than expected for the period of gestation. The foetal parts could not be felt. Vaginal examination revealed the cervix to be 1½ fingers dilated and the membranes were ruptured with a foetal hand and non-pulsatile cord presenting at the cervix. No evidence of placenta praevia was found.

The patient exhibited the picture of concealed and revealed accidental haemorrhage, but at the 19th week of pregnancy.

After 1 pint of Dextran had been given, the cross-matched blood was obtained, and this was transfused into the patient. The first 2 pints were given rapidly followed by a further 2 pints more slowly. The patient's general condition now improved markedly, there was no further vaginal blood loss and the blood pressure remained steady at 100/70. The intravenous transfusion was continued with 5 per cent Dextrose in normal saline slowly whilst the uterine contractions improved.

At 10 p.m. the patient was delivered of a fresh stillborn macroscopically normal foetus. The placenta and membranes were delivered complete 40 minutes later, together with a few ounces of clotted blood. The placenta was circumvallate in type and had a definite depression over four-fifths of its maternal surface where presumably a retroplacental haematoma had lain. Ergometrine 0·5 mg. was given intravenously following the placental

delivery, but the patient continued to lose a steady trickle of blood which formed a very poor clot. The transfusion was therefore changed to a pint of triple strength plasma. (A sample of blood collected just before the plasma was started showed only very poor clot formation after several hours.) The patient continued to have a steady but not heavy loss of blood and 10 ounces of poorly clotted blood were also expelled from the uterus. An intramuscular injection of 5 units Pitocin was given and a short time after this the vaginal bleeding ceased. Following the triple strength plasma, the transfusion was continued very slowly for a further few hours using one bottle of reconstituted single strength plasma, and was then discontinued.

The patient's general condition had deteriorated at the time of the post-abortal haemorrhage, when the blood pressure fell to 90/60, but she soon recovered, and by midnight the blood pressure was steady at her normal level of 115/70.

Blood taken the following morning showed a fibrinogen level of 292 mg. per cent. The patient thereafter progressed satisfactorily. The urinary output was adequate. She was, however, markedly anaemic, with a haemoglobin level of 38 per cent (5·6 g.) on the 2nd post-abortal day. A transfusion of cells from 4 pints of blood was therefore given to the patient, together with 5 daily injections of 5 ml. intramuscular iron. On discharge a few days later the patient was very well and the haemoglobin had risen to 80 per cent (11·8 g.).

Mrs. D. B. attended the Follow-up Clinic on 1st August. She had no complaints and no pelvic abnormality was detected. The haemoglobin level had now risen to 90 per cent (13·3 g.).

## Pathological Report

### *Macroscopical*

A normal looking foetus weighing 280 grams. The crown-rump length is 17 cm. The placenta weighs 110 g.

### *Microscopical*

The foetal lungs are premature in type, and the liver shows much haemopoietic activity. The placental villi are covered by a complete layer of trophoblast. There are fibrinoid deposits on the villi and under the trophoblast; these are fairly frequent. The vessels of the villi are bloodless.

## Comments

The similarity of this case to many other routine abortions is interesting. It emphasizes the need to consider the possibility of hypofibrinogenaemia in all cases of marked uterine bleeding, whether occurring before the 20th week of gestation or later, especially when the uterus shows the characteristics of retroplacental haemorrhage, as in this case. A fibrinogen estimation can then be performed to confirm the diagnosis and the appropriate therapy instituted.

An estimated total of 7½ g. of fibrinogen were given to this patient, but none of it was given as pure fibrinogen. The initial transfusion of 4 pints of blood contained approximately 3 g. of fibrinogen (*Lancet*, 1956). Though this temporarily controlled the blood coagulation defect more fibrinogen was later required and a further 4·4 g. were given in the triple and single strength plasma (Barry, Geoghegan and Shea, 1955).

The retroplacental haemorrhage which killed the foetus and preceded the hypofibrinogenaemia may have been initiated by the circumvallate type of placenta, as suggested by Macafee (1950). Certainly no other evidence was found to account for the premature separation of the normally situated placenta.

## Summary

A case is recorded of hypofibrinogenaemia following retroplacental haemorrhage which occurred at the 19th week of gestation. The foetus was delivered vaginally and had died less than 24 hours earlier. The hypofibrinogenaemia was combated by transfusion of blood and plasma. The need to consider the diagnosis of hypofibrinogenaemia in routine abortions at any gestational age is emphasized.

I should like to express my thanks to Dr. R. Newton for permission to publish this case. I am also indebted to Dr. H. Lempert and Dr. R. F. Jennison for performing the haematological investigations, and Dr. F. A. Langley for the pathological examination.

## References

Barry, A. P., Geoghegan, F., and Shea, S. M. (1955): *Brit. med. J.*, **2**, 287.

*Lancet* (1956): *Lancet*, **1**, 317.

Macafee, C. H. G. (1950): *in* Bowes, K. (ed.): *Modern trends in obstetrics and gynaecology*. Butterworth, London. p. 307.

Veprovsky, E. C., and Levin, A. C. (1956): *Amer. J. Obstet. Gynec.*, **71**, 215.

# SPONTANEOUS REGRESSION OF PULMONARY METASTASES IN A CASE OF CHORIONEPITHELIOMA

BY

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THE following case is reported to illustrate the spontaneous regression of pulmonary metastases of chorionepithelioma following total hysterectomy with bilateral salpingo-oöphorectomy for removal of the primary tumour. The gradual process of resolution was observed over a period of seven months, during which time the general health of the patient improved, the hormonal concentration in the urine fell, cough and blood in the sputum disappeared, and the metastatic lung shadows diminished and finally disappeared.

Park and Lees (1950) estimated that only about 20 cases of claimed regression of pulmonary metastases following hysterectomy for chorionepithelioma have been reported. The ultimate results ascertained in 12 cases showed only clinical evidence—appearance and later cessation of cough and haemoptysis. A few cases were also supported by radiological findings and in 2 cases there was added hormonal evidence. Johnson (1951) reported a case of complete spontaneous regression of the pulmonary metastases with the patient well 15 months after a total hysterectomy and bilateral salpingo-oöphorectomy. Beecham, Peale and Robbins (1955) also reported a case of complete regression of pulmonary metastases but it was attributed to a combination of nitrogen mustard and irradiation therapy. This patient when seen two and a half years after a complete hysterectomy and bilateral salpingo-oöphorectomy was alive and well with no residual disease.

Peightal (1934) reported the only case substantiated by post-mortem findings. X-ray of the lungs of this patient showed evidence of a spontaneous decrease of the size of the pulmonary metastases one and a half months after radium therapy on the uterine lesion and high voltage X-ray therapy on the pelvis. The pelvis was given a second dose after 2 months followed by X-irradiation of the chest, each lung receiving 335 R, but the patient died 2 months later. Post-mortem examination revealed cerebral haemorrhage due to metastases and the lungs were normal except for 5 small nodules of regressing tumour tissue which showed cells similar to those in the brain metastases.

The case reported here appears to be conclusive of spontaneous regression. No treatment was given apart from a total hysterectomy and bilateral salpingo-oöphorectomy.

## CASE REPORT

Mrs. W.P.K., a Chinese married woman, aged 25 years, was admitted to the Queen Mary Hospital on 13th March, 1952. Her chief complaint was recurrent vaginal bleeding for 4 months.

The patient married at the age of 19 and there was nothing of note in the past medical or family history. The menstrual history had previously been normal. Her only child was delivered by breech at full term in 1948.

After a normal 5-days period in October, 1951 she had amenorrhoea for 2 months during which time she experienced the usual signs and symptoms of pregnancy. In December, 1951 she bled once *per vaginam* followed by four attacks in three days in January, 1952, the last of which was accompanied by passage of grape-like material. She was curetted. In February, 1952 (27 days after the termination of the molar pregnancy) she fainted after another attack of severe bleeding, was curetted again, and a mass was said to have been removed from

the uterus. She then developed cough with occasional bloody sputum and a chest X-ray revealed small patches of opacity scattered in both right and left lung fields. She was diagnosed as having pulmonary tuberculosis but no tubercle bacilli could be found in the sputum by the concentration method. In March (51 days after termination of the molar pregnancy) there was yet another attack of vaginal bleeding which was controlled by packing. A few days later she was seen at the University Gynaecological Clinic and admitted to the Queen Mary Hospital.

On admission the patient appeared very pale. The temperature, pulse and respiration were normal and blood pressure 100/66 mm. Hg. The lungs were clear but there was a systolic murmur over the praecordium. There was a moderate degree of tenderness in the lower abdomen and the uterus was soft and enlarged to size of a 3-months pregnancy.

On pelvic examination the external genitals were normal, the fornices clear and the cervix bluish with an erosion of the anterior lip. Chest X-ray (Fig. 1) revealed multiple secondary growths in both lungs and a normal cardiac outline. There was no sugar or albumen in the urine but the urinary chorionic gonadotrophin estimated by Galli-Mainini Test was positive at 1 in 200 dilution and negative at 1 in 500 dilution. The haemoglobin was 58 per cent (8 g. per cent), red blood corpuscles 3,110,000 per c.mm., and white blood corpuscles 6,700 per c.mm.

A diagnostic curettage was planned for 14th March but as soon as the cervix was dilated she bled profusely and curettage had to be abandoned. A blood transfusion was given (500 ml.). Under spinal anaesthesia (heavy nupercaine) a sub-umbilical midline incision was made. The uterus was found to be vascular and soft and enlarged to the size of a 3-months pregnancy. Its peritoneal surface was smooth and there was no evidence of growth penetrating its external surface. The left ovary was slightly smaller than normal and the right ovary cystic. There were no other abnormalities. A total hysterectomy with bilateral salpingo-oöphorectomy was performed, and the patient made an uneventful recovery. She was discharged from hospital on 1st April with the Galli-Mainini Test still positive at 1/20 dilution. Deep X-ray and hormone therapy was not considered as secondary masses in the chest were too extensive.

*Pathology.* Operation specimen consisted of a uterus complete with cervix. Fallopian tubes and ovaries and weighed 77 grammes. There was one firm nodule slightly elevated from the anterior aspect of the left side of the uterus which on section showed a well circumscribed fibromyoma. The uterine cavity measured 7×2 cm. The upper portion was filled with clotted blood covering a rough surface composed of necrotic material to which a few vesicles were attached. A few had infiltrated into the myometrium. Mainly in the fundus were a number of small well circumscribed haemorrhagic areas. Microscopically trophoblastic tissue was seen in the endometrium (Fig. 2). In the myometrium beneath this area were large dark stained cells with bizarre nuclei and there were large and small groups of trophoblast cells within the blood vessels. In some areas, hydatid villi with degenerating cells were found deeply embedded in the myometrium.

The pathological diagnosis was chorionepithelioma of the uterus originating from an infiltrating mole.

On 14th April, 1952 (one month after pan-hysterectomy and 2 weeks after discharge from hospital) patient was re-admitted in a grave condition with intense dyspnoea and extreme pallor with a history that 3 days after discharge from hospital she had an acute attack of severe pain over the right flank which later shifted to the back and right shoulder. It was associated with breathlessness. The symptoms gradually passed off but there were several such attacks later. The last and most severe one occurred a day before re-admission.

On examination, the nail beds and mucous membranes were cyanotic. The temperature was 102·4° F., the pulse 150 per minute and the blood pressure 120/64 mm. Hg. There was diminished air entry on the right side of the chest which was dull on percussion up to the 4th intercostal space posteriorly, the trachea was deviated to the left and coarse rales were heard over the whole of the left side and upper part of the right side of the chest. There were no changes in the heart sounds. Abdominal and pelvic examination showed no evidence of local recurrence of chorionepithelioma.

The haemoglobin was 42 per cent (6·3 g. per cent), red blood corpuscles 2,310,000/c.mm. and white blood corpuscles 14,000/c.mm. The urine was normal except for the Galli-Mainini Test which was positive at 1/10 dilution. X-ray revealed massive effusion (haemothorax) in the right pleural cavity, deviation of mediastinum to the left and further involvement of the left lung by metastases.

The patient was treated symptomatically and given continuous oxygen and her condition remained critical for 3 weeks. During the fourth week, however, there was gradual improvement, the temperature began to settle and the pulse rate decreased. By June, 1952 her temperature and pulse were normal, the haemoglobin 65 per cent (9·8 g. per cent), air entry to the lungs was markedly improved and there was no dyspnoea. X-ray (Fig. 3) showed that fluid in the right pleural cavity was partially absorbed, but the Galli-Mainini Test was still positive at 1/10 dilution. She was discharged from hospital and her health continued to improve. She returned for weekly check up. After 12 weeks the haemoglobin increased to 75 per cent (11·25 g. per cent) and the weight from 67 pounds to 80 pounds and she was able to do light housework.

Figure 4 shows the varying concentration of chorionic gonadotrophins (Galli-Mainini Test) the last result obtained one day before death. There were intermittent negative results since May and the last positive dilution test was at the end of September. The patient continued to have slight cough with blood-stained sputum until November. Comparison X-rays of the chest made monthly showed regression of all the metastases and the last film (Fig. 5) taken one day before death appeared entirely normal.

On 21st December, 1952 she went about her daily routine as usual but complained of being unusually

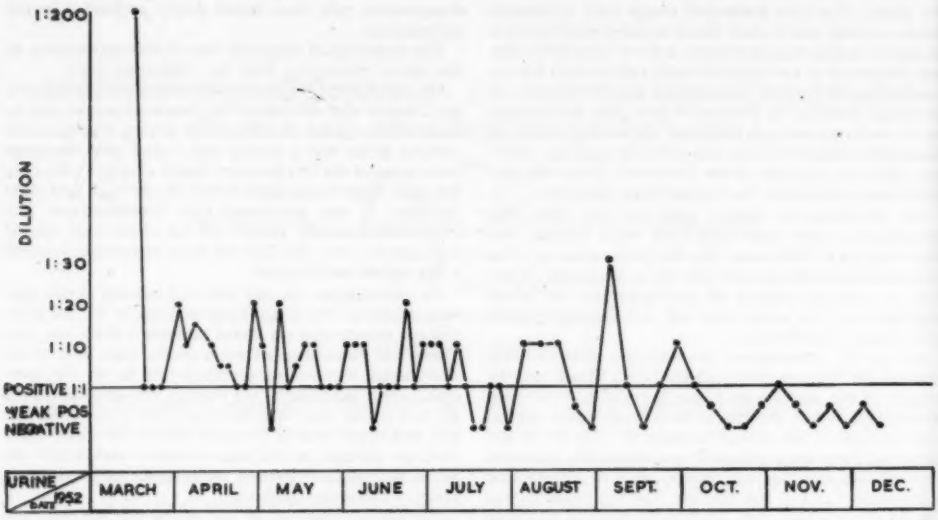


FIG. 4

Graphical illustration of the varying concentration of chorionic gonadotrophins in the patient's urine (as shown by Galli-Mainini test).

tired in the evening. At night she was suddenly seized with a severe headache, was unconscious 20 minutes later and died approximately 2 hours after.

### POST-MORTEM EXAMINATION

Abnormalities were only found in the chest and cranium. The right thoracic cavity was completely obliterated and the viscero-pleura replaced by a thick layer of fibrous tissue with the 3 lobes adherent one to another. These findings are suggestive of the after-effects of haemothorax. The parenchyma was normal except for the presence of 6 small nodules, the largest of which measured 15×12 mm. Several similar nodules were found in the left lung where the visceral and parietal pleura were normal. On section, the nodules were circumscribed and composed of greyish and brownish friable tissues mixed with orange yellow material. Microscopically they were necrotic haemorrhagic areas (Fig. 6) walled off by fibrous tissue and collapsed alveoli. Mononuclear cells and phagocytes were seen loaded with brownish pigmented granules and poorly preserved bizarre nucleated trophoblast cells situated in the lumen of the vessels. Weigert's elastic stain demonstrated clearly the internal elastic laminae indicating metastatic chorionepithelioma in one of the pulmonary arteries. Serial section of the lungs failed to reveal any active trophoblast.

The brain was covered with a layer of blood collected between the soft meninges and brain tissue. There were no other abnormalities and serial section failed to reveal any trophoblastic tissue.

The cause of death was subarachnoid haemorrhage. There was regression of pulmonary metastatic chorionepithelioma.

### DISCUSSION

The diagnosis of chorionepithelioma of the uterus with pulmonary metastases and the regression of the latter were based on the following:

(1) Clinical evidence.
(2) Radiological evidence in the chest.
(3) Biological tests.
(4) Histopathology of the uterus.
(5) Post-mortem evidence.

(1) *Clinical evidence.* After termination of a

FIG. 2
Shows trophoblastic tissue in the endometrium.



FIG. 1
Shows multiple bilateral pulmonary metastases.

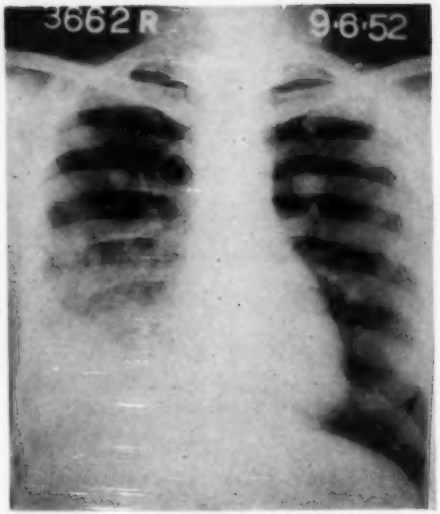


FIG. 3

Shows pleural effusion and reduction in size of bilateral pulmonary metastases.

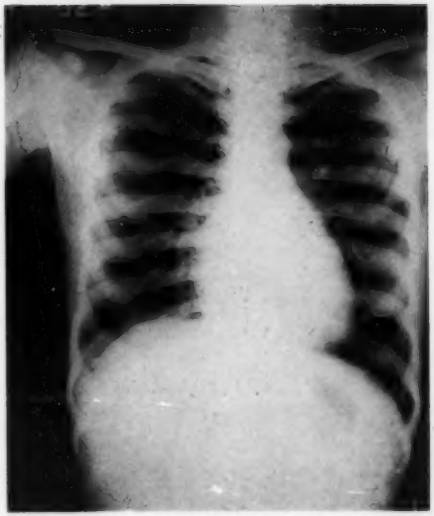

FIG. 5

Shows disappearance of the pulmonary metastases.

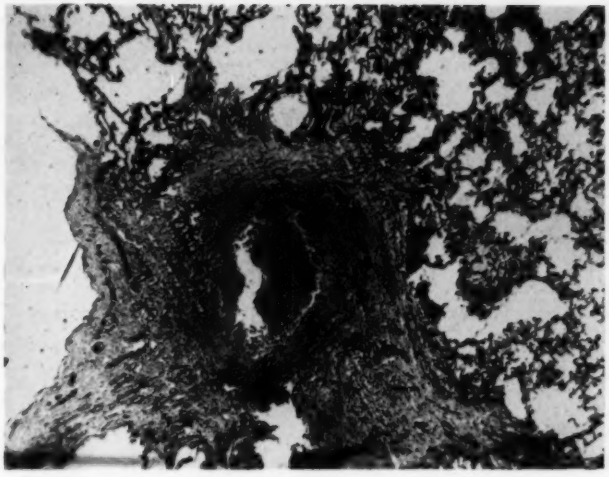

FIG. 6

Shows a necrotic haemorrhagic area walled off by fibrous tissue and collapsed alveoli in the lung.

molar pregnancy the patient continued to have intermittent attacks of vaginal bleeding in spite of repeated curettages. The subsequent development of cough with blood in sputum was consistent with the presence of pulmonary metastases, the regression of which was indicated by the gradual disappearance of chest symptoms and the improvement of the general condition of the patient.

(2) *Radiological evidence in the chest.* There were well circumscribed multiple nodular densities throughout both lung fields (Fig. 1 taken on 13th March, 1952). X-ray examination made on 15th April, 1952 showed marked right pleural effusion, evidently secondary to pleural involvement. From 9th June, 1952 onwards serial films showed gradual subsidence of the effusion and disappearance of the rounded opacities (Fig. 5).

(3) *Biological tests.* Figure 4 illustrates the varying concentration of chorionic gonadotrophins in the patient's urine. The marked initial drop from 1:200 to 1:1 positive dilution test was due to the removal of the chief source of hormone production from the growth in the uterus. The presence of metastases was responsible for the persistence of positive results many months after operation. *Pari passu* with the clinical improvement of the general health of the patient the weakening of the tests shown in the latter part of the graph was indicative of retrogression of metastases.

(4) *Histopathology.* The presence of anaplastic trophoblastic tissue in the uterine muscle and blood vessels confirms the diagnosis of chorionepithelioma.

(5) *Post-mortem evidence.* Figure 6 shows convincing evidence that regression had taken place in the pulmonary metastatic nodules. It was interesting to note that the patient died of cerebral haemorrhage and that thorough investigation failed to reveal the cause of it although one cannot rule out entirely the presence of minute cerebral metastasis.

Generally speaking, chorionepithelioma is one of the most malignant tumours and yet in rare instances it shows regression not only in the metastases but also in the primary growth. Novak and Koff (1930) reported a case in which the primary tumour had disappeared with death from metastases. The regression of vulvo-vaginal metastases has been observed by Brews (1950) and many others. Brews reported a 10-year cure of a case of regression of vulvo-vaginal and pulmonary metastases after hysterectomy. In other malignant tumours, however, such events are extremely rare. Chorionepithelioma is a neoplastic lesion of the trophoblast or foreign tissue of the body whereas in other tumours they originate from the host cells. In normal pregnancy chorionic villi have been observed in the pulmonary tissue and it is believed that a certain lytic substance present in pregnant woman dissolves these wandering villi. Similarly in chorionepithelioma it may stimulate the production of certain substances which destroy the tumour, but the usual outcome is that the tumour grows faster than the production of lytic substance so that the victims are usually killed. Another explanation of regression is death of cells from cutting off of blood supply. It is common knowledge that chorionepithelioma proliferates and erodes blood vessels (shown by the extensive haemothorax in the present case) so that the lesion is mixed and/or surrounded by effused blood. If it is completely surrounded the trophoblast must die when nutrition is exhausted. Should a lesion be partially surrounded by blood, the blood supply is still available and the lesion will survive and proliferate. These are the theories propounded but the actual mechanism is still unknown.

Since no metastases were found in the brain the cerebral haemorrhage might be due to other causes such as congenital defect of cerebral vessels, but the presence of metastases cannot be entirely excluded in view of the Galli-Mainini Tests which were occasionally weakly positive before death.

## Summary

(1) A case of spontaneous regression of pulmonary metastatic growth of chorionepithelioma following removal of primary tumour in the uterus was described.

(2) The patient lived 11 months after termination of molar pregnancy, 9 months after hysterectomy and 7 months after appearance of regression of metastases.

(3) The diagnosis of chorionepithelioma, presence of pulmonary metastases and regression of the latter were discussed based on the clinical, biological, radiological, histological and post-mortem findings.

(4) The cause of cerebral haemorrhage which was responsible for death was not found in the post-mortem examination.

(5) The mechanisms of regression were discussed.

## References

Beecham, C. T., Peale, A. R., and Robbins, R. (1955): *Amer. J. Obstet. Gynec.*, **69**, 510.

Brews, A. (1950): *J. Obstet. Gynaec. Brit. Emp.*, **57**, 317.

Johnson, W. R. (1951): *Amer. J. Obstet. Gynec.*, **61**, 701.

Novak, E., and Koff, A. K. (1930): *Amer. J. Obstet. Gynec.*, **20**, 153.

Park, W. W., and Lees, S. C. (1950): *Arch. Path.*, **49**, 73, 205.

Peightal, T. C. (1934): *Amer. J. Obstet. Gynec.*, **28**, 435.

# COILING OF THE UMBILICAL CORD AROUND THE FOETAL NECK

BY

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IN teaching medical students and nurses, as well as for other purposes, it is sometimes helpful to know with some degree of accuracy and documentation certain elementary facts about coiling of the umbilical cord around the foetal neck. Such facts are: the frequency with which one coil, two coils and three or more coils, are encountered; the bearing, if any, of cord length on coiling, and more important, the bearing, if any, of coiling on foetal prognosis.

A survey of a number of British and American textbooks has yielded scant information on this subject. Based on clinical impressions, the estimates given of the incidence of the phenomenon in general vary from once in three cases to once in six; but no details are mentioned and no references to the literature cited. The only other pertinent statement found, made in many textbooks, is that coiling of the cord around the neck may cause "strangulation" of the foetus. This explanation of foetal loss, when no other cause of death is evident, appears to be widely accepted, especially when the cord is both coiled and short.

In order to investigate these several aspects of coiling of umbilical cord, a study was made of 1,000 consecutive deliveries at the Tsan Yuk Hospital, Hong Kong. Since 7 twin pregnancies occurred in the series, the total number of infants and cords was 1,007. Although routine measurements of cord length are made in many obstetrical laboratories, such data are of little value for the purpose at hand, because they do not include as a rule the segment of cord left on the infant, which may vary greatly from case to case and from clinic to clinic. Accordingly, this specific investigation was undertaken. One of us (K.P.S.) stressed to the house staff, midwives and medical students assigned to the delivery suites the importance of accurate observations on cord coiling and cord length for the purposes of this study and himself supervised and checked a large portion of the measurements.

As may be seen in Table I, the incidence of one loop of cord around the neck was about 20 per cent and that of two loops, 2·5 per cent. The 2 cases in which three coils were around the neck are obviously inadequate for evaluation but the frequency of triple coiling may well be of this general order, that is, once in some five hundred cases.

Table I shows also that a certain correlation exists between average cord length and the number of coils around the neck. As demonstrated by the standard errors, the increased cord length in the "one-coil" group over the length in the "no-coil" group is unquestionably a valid observation; and there are seven chances in eight that the next difference shown, between cord length in the "one-coil" and "two-coil" groups, is not a sampling error. Although no particular weight can be attached to the two extremely long cords in the two "three-coil" cases, it is of interest that in still another "three-coil" case, observed since this series was completed, the cord was 76 cm. in length. All in all,

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TABLE I

*Incidence of Coiling of Umbilical Cord in 1,000 Consecutive Deliveries (Including Seven Sets of Twins) and the Average Cord Length in Respect to Degree of Coiling*

| Coils of Cord Around Neck | Number of Infants | Per cent | Average Cord Length | |
|---|---|---|---|---|
| | | | Cm. | Standard Error |
| None .. .. | 772 | 76·7 | 44·9 | 0·3 |
| One .. .. | 208 | 20·6 | 50·8 | 0·7 |
| Two .. .. | 25 | 2·5 | 54·3 | 2·2 |
| Three .. .. | 2 | 0·2 | 79·5 | — |
| Total .. | 1,007 | 100·0 | 46·4 | — |

the trend shown in Table I toward increased cord length *pari passu* with the degree of coiling affords some factual basis for the belief that excessive cord length is an important predisposing cause of coiling.

On the other hand, coiling may occur with short cords. Thus, in our "one-coil" series of 208 cases, the length of the cord was less than 40 cm. in 23 cases and was less than 45 cm. in 5 of the "two-coil" group.

Table II does not justify the tendency to attribute otherwise unexplained foetal deaths to coiling of the cord around the neck. This is certainly true in regard to "one-coil" cases because our perinatal mortality in that group, despite the presence of 23 cords under 40 cm. in length, was no higher than that in the "no-coil" category. In this connexion, it should be recalled that about one-half of all foetal deaths, with or without loops of cord around the neck, are without explanation, despite careful autopsy studies. To demonstrate convincingly that the perinatal mortality in cases with two or more loops around the neck is comparable to that in cases with no coiling would require a series ten

TABLE II

*Foetal and Neonatal Death Rate According to Degree of Coiling of Umbilical Cord Around Foetal Neck*

| Coils of Cord Around Neck | Number of Infants | Total Foetal and Neonatal Deaths | |
|---|---|---|---|
| | | Number | Per cent |
| None .. .. .. | 772 | 20 | 2·6 |
| One .. .. .. | 208 | 2 | 1·0 |
| Two .. .. .. | 25 | 0 | 0·0 |
| Three .. .. .. | 2 | 0 | 0·0 |
| Total .. .. | 1,007 | 22 | 2·2 |

or more times the size of this one; and in any event it is not our intention to maintain that coiling of the umbilical cord is *never* a cause of infant loss. However, the data presented would seem to show quite clearly that coiling must be a rare cause of perinatal death and that the lethal role assigned to it has been exaggerated.

## SUMMARY

(1) In 1,000 consecutive deliveries at the Tsan Yuk Hospital, Hong Kong, the incidence of coiling of the umbilical cord around the foetal neck was: one loop, 20·6 per cent; two loops, 2·5 per cent; and three loops, two times.

(2) A certain correlation was demonstrated between cord length and the number of loops around the neck; and cord length is undoubtedly an important predisposing factor, but the phenomenon occurs occasionally with short cords.

(3) The stillbirth and neonatal death rates were no higher in the "coiled" cases than in the "non-coiled" and the conclusion is reached that coiling of the umbilical cord around the foetal neck, even in cases of short cords, is rarely a cause of perinatal death.

# SPINAL ANALGESIA AND CAESAREAN SECTION

## Maternal Mortality

BY

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WHEN ether and chloroform were the choice of general anaesthetics, the uterine atony and tendency to haemorrhage following the administration of these agents stood in sharp contrast to the increased uterine tone associated with spinal analgesia. In addition, the latter is attended by a smaller incidence of respiratory dysfunction in the foetus and produces superior operating conditions. Indeed, had it not been for occasional reports of sudden and fatal circulatory collapse occurring during Caesarean section performed under spinal block, it is likely that there would have been few advocates for general anaesthesia for this operation. It is because of this danger and since the advent of general anaesthetic methods, which are capable of avoiding uterine atony and producing more favourable conditions both for the surgeon and the foetus, that spinal analgesia has become regarded by many as an unjustified procedure if an up-to-date anaesthetic service is available.

However, it is the belief of a number of obstetricians and anaesthetists that general anaesthesia, whatever the agent, is a handicap to the baby (Mayer, 1928; Batten, 1943; Resnick, 1945; Heard, 1946; Cave, 1947; Paton, 1947; Andros *et al.*, 1948; Lull and Hingson, 1948; Davenport and Prime, 1950; Held, 1950; Neme, 1950; Koenig, 1951) and that it should definitely be avoided when dealing with a premature or distressed foetus (Eisenberger, 1932; Acken, 1947; Marshall, 1947; Thomas, 1947; Eastman, 1948; Masters and Ross, 1949; Lull and Ullery, 1949; Downing, 1951; Potter and Pender, 1951; De Carle, 1954). For this reason, it is regrettable that subarachnoid block —the simplest, quickest and most efficient method of inducing regional analgesia—has fallen from favour for the operation in which it can have particular merits.

Few subjects have given rise to sharper controversy and more confusion of thought than spinal analgesia for Caesarean section. On the one hand, there is the widely held view that pregnancy, particularly in the latter weeks, is in itself an absolute contra-indication to the use of spinal block because of the fatalities which have occurred. However, the cause of these deaths has never been demonstrated satisfactorily. On the other hand, it is the opinion of those who have employed this technique in a great number of cases without accident that it is entirely safe. McIntosh Marshall (1939) reviews the large volume of reports up to 1939 without prejudice and comes to the conclusion that a death rate of at least 1 per cent is inevitable.

### AETIOLOGY

In an endeavour to substantiate a susceptibility to spinal analgesia, supposedly peculiar to women in the late weeks of pregnancy, a variety of physiological and biochemical changes associated with gestation have been cited. The numerous theories, advanced from time to time, are too well known to require further reference. Anderson (1946) discusses most of these hypotheses—some far-fetched—and dismisses the majority clearly and convincingly. One can only agree with Macintosh and Mushin (1944) when they state: "On common sense grounds it appears to us to be a bogey to suggest that pregnancy makes a woman peculiarly susceptible to the effects of spinal analgesia." A theory which found some acceptance concerns the effects of restlessness and uterine contractions

on cerebrospinal fluid pressure (Franken, 1934). The increased pressure in the subarachnoid space was thought to assist an abnormally rapid cephalic spread of the analgesic agent and thus cause extensive sympathetic block and paralysis of the intercostal muscles. Vehrs (1934), however, states that it is more difficult to attain subdural block of the thoracic segments in patients with a high cerebrospinal fluid pressure. In any case, not all the fatalities occurred in women who were in labour at the time of section. Macintosh (1949) is of the opinion that the cause is to be found in paralysis of the intercostal muscles and diaphragmatic dysfunction and this is illustrated by Case No. 1 of those described by Van der Post (1938) in which "air hunger" developed 30 minutes after induction of spinal block. However, it is a feature of the majority of reports that collapse took place very soon after the subarachnoid injection, often before the operation had begun, and it does not appear that sufficient time had elapsed for respiratory inadequacy to have proved fatal. The question also comes to mind how a conscious and usually perfectly fit patient dies from anoxia without exhibiting unmistakable signs of respiratory and mental distress. These deaths are described as being sudden and unheralded.

It has been possible to cull from the literature eleven reports (Babcock, 1932; Katz, 1933; Feiner, 1936; Lienhoop, 1936; Brochier and Ambre, 1937; Cotte and Banssillon, 1937; Ginglinger, 1937; Mygind, 1945; Brown, 1946; Walker and Matthews, 1950; Baden and Baden, 1953) giving some detail of the circumstances leading to fatal circulatory collapse in 17 cases; they reveal a definite pattern. Sudden death occurred some minutes after the patient had been placed in the supine position following a subarachnoid injection. The interval depended on the analgesic drug employed and was closely related to the time which the agent in question usually takes to produce sympathetic block of the thoracic segments. Two further points are evident from the study of these reports: firstly, that the beginning of circulatory deterioration was not appreciated (cessation of respiration was usually the first untoward sign observed), and, secondly, that measures of resuscitation were ineffectual and not guided by an understanding of the situation. The former can probably be explained by the common practice in which the surgeon induced spinal analgesia and then proceeded to undertake the operation, there being no critical supervision of the patient's condition. The fact that respiratory arrest was usually the first indication of trouble doubtless led to the belief that the condition was primarily one of peripheral respiratory paralysis due to an abnormally high subarachnoid block when, in fact, it was a terminal phenomenon.

Two of these reports (Katz, 1933; Baden and Baden, 1953) mention a steep fall of pulse rate, one from 150 to 54, the other from an unrecorded rate to 48 per minute. These are significant observations suggesting incomplete cardiac filling due to a reduced venous return. In addition to the fatal cases referred to, Dolff (1950) describes 3 cases of "severe, dangerous circulatory collapse, with cessation of respiration" shortly after placing the patient in the supine position following induction of spinal block. All 3 patients recovered but unfortunately the resuscitative measures are not mentioned.

The work of Brigden, Howarth and Sharpey-Schäfer (1950) suggests the real cause of these fatalities and fits well into the clinical picture. These authors demonstrate that women in late pregnancy exhibit, in the supine position, a rise of venous pressure in the legs of 7·5 cm. (measured by condensor manometer) and that this rise can be reduced considerably by turning the subject slightly to one side. They also quote a personal communication by Palmer and Walker who found that arterial pressure fell in women in late pregnancy after they assumed the recumbent position. Hansen (1942) noted "in the last month of pregnancy a marked predisposition to collapse in the supine position. This disturbance vanishes when the patient moves into the left lateral position."

The fact that the high venous pressure in the lower extremities is reduced significantly by turning the subject slightly to one side suggests that this phenomenon is caused by pressure of the enlarged uterus on the inferior vena cava. Such an interference with venous return to the heart will produce a fall of cardiac output and arterial pressure. There is also some evidence that, apart from the pressure exerted by the

uterus, a postural factor predisposes to obstruction of flow through the inferior vena cava because Brigden *et al.* (1950) showed that some subjects will experience a rise of venous pressure in the legs and faint when adopting, in the erect position, the abnormal lordosis seen in pregnancy. One individual exhibited a steady rise of heart rate to 180 per minute, followed by a sudden fall to 40 per minute and became unconscious after assuming a lordotic posture. This must be taken as clear evidence of retarded cardiac filling. If a considerable reduction of vasomotor tone, as a result of spinal block, is induced in such patients, a dangerous fall of cardiac output can be brought about. However, this will only occur in those subjects in whom these mechanical factors are present to a marked degree and whose vasomotor systems are extensively blocked. Most authors who report large series of Caesarean sections under spinal analgesia without maternal mortality employed relatively small doses of the analgesic agent resulting in minimal vasomotor paralysis.

The following case report which illustrates this phenomenon may be of interest.

A woman, aged 40, of good general health, was brought to theatre at term for elective lower segment Caesarean section which was indicated by disproportion and previous section. Her blood pressure, taken on a number of occasions, had varied between 120/75 and 100/60 mm. Hg. The pulse rate had been between 100 and 108 per minute.

Arriving for the proposed operation, the anaesthetist (not the writer) saw the patient lying in the supine position on the operating table, rather restless and being controlled by two nurses. On being questioned, she complained of feeling faint. Her systolic blood pressure was assessed at 40 mm. Hg. A physician confirmed this reading, and, unable to find a cause, recommended that the operation should be postponed.

The writer was consulted later the same day with a view to giving the anaesthetic on the following morning. This was agreed to after the blood pressure reading, carried out while the patient sat on a chair, was found to be 130/85 mm. Hg.

On arrival in the theatre, the patient was seen lying in the lateral position on the operating table resisting the nurse's attempts to induce her to lie on her back. When questioned, she explained her reluctance by stating that she felt faint on her back but all right on her side. The blood pressure was taken in both positions and estimated to be 40/? and 120/80 mm. Hg respectively, while in the supine position with one loin raised on a pad, it was 90/65 mm. Hg.

Anaesthesia was induced with 250 mg. thiopentone and 10 mg. d-tubo-curarine chloride while the patient lay on her side. Once unconscious, she was turned on to her back, her left loin slightly raised, and the administration of 50 per cent nitrous oxide and oxygen begun. At this stage her blood pressure was 80/60 mm. Hg. After evacuation of the uterus cyclopropane and oxygen were given for the remainder of the operation, during which time the blood pressure remained at 120/80 mm. Hg. Post-operative progress was uneventful and alterations of posture produced no further fluctuations in the blood pressure.

It is obvious that an extensive sympathetic block could have had disastrous results in this patient.

## Comment

Careful pre-operative investigation will reveal the patient who exhibits circulatory lability in the supine position. Proper dosage of the analgesic drug and avoidance of barbotage will prevent a dangerous extent of vasomotor paralysis. Vigilant supervision will focus attention on an early decline of cardiac output, in which case venous return and cardiac filling can be restored by turning the patient on to one side and raising her legs.

## Conclusions

It is suggested that: (1) the mechanism in sudden circulatory collapse during Caesarean section under spinal analgesia is a combination of the effects of occlusion of the inferior vena cava and reduction of peripheral vascular resistance on cardiac output.

(2) It should be possible to foresee this danger, hitherto thought unpredictable, as a result of pre-operative examination.

(3) The use of subarachnoid block in Caesarean section is safe if the principles which have been outlined are understood and observed.

## Acknowledgment

I wish to thank Dr. Douglas Miller for his permission to publish the case report.

## References

Acken, H. S. (1947): *Amer. J. Obstet. Gynec.*, **53**, 927.

Anderson, A. F. (1946): *J. Obstet. Gynaec. Brit. Emp.*, **53**, 347.

Andros, G. J., Dieckmann, W. J., Ouda, P., Priddle, H. D., Smitter, R. C., and Bryan, W. M., Jr. (1948): *Amer. J. Obstet. Gynec.*, **55**, 806.

Babcock ,M. E. (1932): *Curr. Res. Anesth.*, **11**, 184.

Baden, E. E., and Baden, W. F. (1953): *Amer. J. Obstet. Gynec.*, **66**, 202.
Batten, D. H. (1943): *Curr. Res. Anesth.*, **22**, 143.
Brigden, W., Howarth, S., and Sharpey-Schäfer, E. P. (1950): *Clin. Sci.*, **9**, 79.
Brochier and Ambre (1937): *Bull. Soc. Obstét. Gynéc., Paris*, **26**, 588.
Brown, A. E. (1946): *Med. J. Aust.*, **2**, 488.
Cave, J. N. (1947): *Proc. R. Soc. Med.*, **40**, 566.
Cotte and Banssillon (1937): *Bull. Soc. Obstét. Gynéc., Paris*, **26**, 589.
Davenport, H. T., and Prime, F. J. (1950): *Brit. med. J.*, **1**, 1347.
De Carle, D. W. (1954): *J. Amer. med. Ass.*, **154**, 545.
Dolff, C. (1950): *Geburtsh u. Frauenheilk.*, **10**, 915.
Downing, G. C. (1951): *West. J. Surg. Gynec. Obstet.*, **59**, 19.
Eastman, N. J. (1948): *Amer. J. Dis. Child.*, **76**, 661.
Eisenberger, F. (1932): *Zbl. Gynäk.*, **56**, 3024.
Feiner, D. (1936): *Amer. J. Obstet. Gynec.*, **32**, 1001.
Franken, H. (1934): *Zbl. Gynäk.*, **58**, 2191.
Ginglinger, A. (1937): *Bull. Soc. Obstét. Gynéc., Paris*, **26**, 367.
Hansen, R. (1942): *Klin. Wschr.*, **21**, 241.
Heard, K. M. (1946): *Curr. Res. Anesth.*, **25**, 191.
Held, E. (1950): *Gynaecologia, Basel*, **130**, 364.
Katz, H. (1933): *Arch. Gynäk.*, **152**, 332.
Koenig, F. E. (1951): *Gynaecologia, Basel*, **131**, 208.
Lienhoop, F. (1936): *Schmerz, Narkose-Anaesthie*, **9**, 145.
Lull, C. B., and Hingson, R. A. (1948): *Control of pain in childbirth*. Lippincott, Philadelphia. p. 434.
Lull, C. B., and Ullery, J. C. (1949): *Amer. J. Obstet. Gynec.*, **57**, 1199.
Macintosh, R. R. (1949): *Brit. med. J.*, **1**, 409.
Macintosh, R. R., and Mushin, W. W. (1944): *Lancet*, **2**, 675.
Marshall, C. M. (1939): *Caesarean section: lower segment operation*. Wright, Bristol. p. 66.
Marshall, C. M. (1947): *Proc. R. Soc. Med.*, **40**, 560.
Masters, W. H., and Ross, R. W. (1949): *J. Amer. med. Ass.*, **141**, 909.
Mayer, A. (1928): *Zbl. Gynäk.*, **52**, 2490.
Mygind, H. B. (1945): *Ugeskr. Laeg.*, **107**, 489.
Neme, R. (1950): *Obstet. Ginec. lat.-amer.*, **8**, 475.
Paton, C. N. (1947): *Med. J. Aust.*, **2**, 289.
Potter, J. K., and Pender, B. H. (1951): *Curr. Res. Anesth.*, **30**, 35.
Resnick, L. (1945): *Brit. med. J.*, **2**, 722.
Thomas, R. C. (1947): *Proc. R. Soc. Med.*, **40**, 557.
Van der Post, C. W. H. (1938): *Brit. J. Anaesth.*, **15**, 117.
Vehrs, G. R. (1934): *Spinal anesthesia: technic and clinical application*. Kimpton, London. p. 121.
Walker, A. H. C., and Matthews, S. (1950): *Brit. med. J.*, **1**, 938.

# FOETAL DISTRESS AND NEONATAL ASPHYXIA

BY

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## PART I

WITH improvements in maternal obstetric management, it is possible to turn increasingly to the care of the child, especially throughout labour and in the immediate postnatal period, when the child is at greatest risk. Though the signs considered to indicate foetal distress have been recognized for many years, it is, however, also necessary to assess the urgency and the severity of the threat to the child's life, for, although the majority of babies recover quickly at birth, any tendency to foetal asphyxia is evidence that the margin of safety has been reduced.

It is the purpose of this investigation to determine the incidence and evaluate the significance of the various classical signs of foetal distress, to correlate the occurrence of these signs with the incidence of foetal asphyxia at birth, and to consider whether it is desirable to take into account minor deviations from normal.

### MATERIAL AND METHODS

Consecutive cases of women in labour were taken for the investigation. Records were made by medical and nursing staff of the foetal heart rate and rhythm at hourly intervals during the first stage of labour, and at 15-minute intervals throughout the second stage. The presence of meconium was noted, and careful observations were made concerning the maternal condition and the type of uterine contractions. A small number of cases were discarded where records of the mother or the baby were inadequate, and those in which the foetal heart was lost before the onset of labour.

The report is based upon observations made on 1,000 patients delivered at the Maternity Hospital at Leeds. These deliveries resulted in 1,005 live births; there were 17 twins, and 12 babies were stillborn.

Foetal distress and significant changes in foetal heart rate were noted in 29·9 per cent of all cases, an incidence of foetal distress considerably higher than that recorded by the majority of other workers. It is probable that the stringent interpretation of the terms foetal distress and asphyxia employed in the present investigation accounts for this difference.

The literature contains few attempts at a precise definition of neonatal asphyxia. Experience in the present investigation showed that the newly-born infant's colour, cry and muscle tone were too dependent on variable subjective opinion to be of value. It was found that the first gasp often occurred within moments of birth in infants who by other criteria were severely asphyxiated. The majority of healthy babies born at term, and whose delivery was uncomplicated, commenced to breathe regularly within one minute of birth, and for the purpose of this investigation, therefore, the fact that breathing had or had not started within one minute of birth was accepted as a reliable criterion of normal behaviour or asphyxia. Using this definition, asphyxia was noticed in 24·4 per cent of those babies born alive.

### I. RISE IN FOETAL HEART RATE

In his classic description of foetal distress, von Winckel (1903) attached significance to a rise in foetal heart rate to 160 per minute. It was felt that changes in foetal heart rate from a level that had been sustained for some time, but were of lesser degree, were also significant, and that a rise of 20 or more, even though the rate did not

exceed 160 per minute, should be considered evidence of foetal distress. In order to secure this base line in foetal heart rate, records were begun early in labour, and at a time when the strength of uterine contractions and the intact membranes had minimal effect on the foetus. This ensured that any decrease or increase in foetal heart rate occurring before a critical level was reached did not pass unnoticed. (Table I.)

(*a*) A rise in foetal heart rate alone to 160 per minute or more occurred less frequently than in association with other manifestations of distress, and only in 21 cases was it the sole finding. Asphyxia was present in 7 (35·0 per cent) of the babies who survived, and 1 was stillborn. In a further 26 cases additional signs of distress were noted, and of these 13 babies showed asphyxia, and 1 was stillborn, making the incidence of asphyxia at birth in the whole group of 45 babies who lived to be 44·4 per cent. Breathing was delayed to 5 minutes in 8 babies, an incidence of severe asphyxia of 22 per cent.

(*b*) When the rise was 20 or more, but not exceeding 160, from a previously sustained rate, asphyxia was demonstrated in 7 (30·4 per cent) of 23 babies born alive. Meconium was passed in an additional 6 cases, of which 3 babies showed asphyxia at birth and there was 1 stillbirth. It would seem that a rise of 20 per minute in foetal heart rate is significant.

### II. Fall in Foetal Heart Rate

A fall in foetal heart rate below 100 per minute has been regarded as indicative of foetal distress, but in this investigation the effect on the foetus of a fall in heart rate of 20 from a previously sustained level has also been examined. (Table II.)

(*a*) In 19 cases there was a fall in foetal heart rate below 100 per minute as the one sign of distress, and 4 of these babies (21 per cent) showed asphyxia at birth. A fall in foetal heart rate was accompanied by additional signs of foetal distress in a further 46 cases, the onset of regular respiration being delayed in 26 (41·9 per cent) of the whole series, and 3 babies in this last group were stillborn.

(*b*) The 68 cases in which the fall in foetal heart rate was 20 or more from a maintained level, but not below 100, gave an incidence of asphyxia of 22 cases (32·3 per cent). In an additional 12 patients, in whom meconium was passed and a fall in foetal heart rate of 20 noted, 4 babies showed evidence of asphyxia.

Table I

*Relation Between Rise in Foetal Heart Rate and Asphyxia at Birth*

| | No. of Cases | Asphyxia | Asphyxia (Per cent) |
|---|---|---|---|
| Rise to 160+ | 20+1 SB. | 7 | |
| Rise to 160 and other F.H. changes | 16 | 7 | 44·4 |
| Rise to 160 and Meconium | 9+1 SB. | 6 | |
| Rise of 20 plus Meconium | 5+1 SB. | 3 | — |
| Rise of 20 per minute | 23 | 7 | 30·4 |

Table II

*Relation Between Fall in Foetal Heart Rate and Neonatal Asphyxia*

| | No. of Cases | Asphyxia | Asphyxia (Per cent) |
|---|---|---|---|
| Fall below 100 | 19 | 4 | |
| Fall below 100 and other changes | 27 | 12 | 41·9 |
| Fall below 100 and Meconium | 16+3 SB. | 10 | |
| Fall of 20 and Meconium | 12 | 4 | — |
| Fall of 20 | 68 | 22 | 32·3 |

### III. Fluctuations and Irregularities of Foetal Heart Rate

The term fluctuation has been applied to the slow variations in foetal heart rate with gradual rise and fall over a range of 25 beats or more, whereas finer irregularities, missed beats and alterations in rate with uterine contractions are grouped as irregularities.

Table III
*Association of Fluctuating Foetal Heart Rate and Asphyxia*

| | No. of Cases | Asphyxia | Asphyxia (Per cent) |
|---|---|---|---|
| Fluctuations only .. .. | 38 | 17 | 44·7 |
| Fluctuations and other signs | 56 | 29 | 51·8 |

(*a*) Table III summarizes the association between fluctuations in foetal heart rate and asphyxia at birth. In 38 charts fluctuations alone were noticed, in some cases the range being gross, and of these 17 babies (44·7 per cent) were slow to breathe, 7 taking over 5 minutes before the onset of regular respiration. Fluctuations were often one of multiple signs, and in these 56 cases asphyxia was present at birth in 29 (51·8 per cent).

(*b*) Irregularities of rhythm were noticed in only 1 instance as the sole sign of foetal distress, but it presented as an additional factor in 20 other cases.

### IV. Meconium

The passage of meconium as a sign of foetal distress is well recognized, and often it may be the earliest evidence. In practice the warnings of distress were frequently found to be multiple, meconium being accompanied by alterations in both foetal heart rate and rhythm.

Meconium was passed in 35 cases in the absence of any alteration in foetal heart rate, 17 of these babies (50 per cent) were slow in breathing, and there was 1 stillbirth. In an additional 53 cases the passage of meconium was associated with changes in foetal heart rate. Twenty-four (50 per cent) of the 48 babies born alive showed a degree of asphyxia, there were 5 stillbirths and asphyxia was severe in 19 per cent of the whole group of 82 babies.

### V. Multiple Signs of Foetal Distress

Multiple signs of foetal distress were present in 96 cases, and of these babies, 5 were stillborn and 45 (46·8 per cent) showed asphyxia at birth.

### VI. No Evidence of Foetal Distress

No foetal heart changes and no meconium were found in 701 patients with an incidence of neonatal asphyxia of 17·7 per cent, and severe asphyxia of 5·1 per cent. In the 5 instances in which sudden cessation of the foetal heart occurred, it was felt that more frequent scrutiny might have produced a warning, though seldom in time for effective treatment.

Table IV
*Comparison of the Various Signs of Foetal Distress With the Incidence of Neonatal Asphyxia*

| | No. of Cases | Asphyxia (Per cent) |
|---|---|---|
| Rise to 160 (all cases) .. .. | 45 | 44·4 |
| Fall to 100 (all cases) .. .. | 62 | 41·9 |
| Meconium (all cases) .. .. | 82 | 50·0 |
| Fluctuations (all cases) .. | 94 | 48·8 |
| Rise of 20 .. .. .. .. | 23 | 30·4 |
| Fall of 20 .. .. .. | 68 | 32·4 |
| No sign of foetal distress .. | 701 | 17·7 |

## PART II

The second part of this paper consists of an analysis of various obstetric factors and their relationship to foetal distress and asphyxia of the child at birth.

### I. Maternal Age

The influence of maternal age on foetal distress and neonatal asphyxia is linked to a

Table I
*The Influence of Maternal Age on the Incidence of Foetal Distress and Neonatal Asphyxia*

| Maternal Age | Under 25 Years | 25–34 Years | Over 35 Years |
|---|---|---|---|
| No. of Cases .. .. | 371 | 505 | 112 |
| Foetal distress (per cent) .. | 30·5 | 27·6 | 29·2 |
| Asphyxia (per cent) .. | 20·8 | 23·2 | 32·2 |

considerable extent with parity, the majority of patients under 25 years of age being primiparae.

In this series, the incidence of foetal distress was not affected by maternal age, but asphyxia at birth was encountered more frequently in infants born to mothers of 35 years or more. Twenty-nine patients who were over 35 years of age were pregnant for the first time, and in this group of elderly primiparae there were 12 cases (41 per cent) of foetal distress and 11 cases (38 per cent) of asphyxia at birth. Although these figures are small, they show an increase in both factors.

## II. Parity

Foetal distress and neonatal asphyxia were both more frequent in first pregnancies, but in succeeding pregnancies after the seventh asphyxia again became noticeable, its incidence equalling that in the first pregnancy.

Table II
*Incidence of Foetal Distress and Asphyxia at Birth in Primiparae and Multiparae*

| | Para-1 | Para-2 or More |
|---|---|---|
| No. of cases .. .. .. | 687 | 313 |
| Foetal distress (per cent) .. | 33 | 23·3 |
| Asphyxia (per cent) .. .. | 25·6 | 20·8 |

## III. Maturity

### (a) *Prematurity*

There were 108 infants who weighed 5½ pounds or less at birth. The incidence of foetal distress, and more particularly asphyxia of the child at birth, bore a close relation to the birth weight.

Table III
*Relationship of Foetal Distress and Asphyxia to Birth Weight in Premature Infants*

| | Under 3½ Pounds (16 Infants) | 3½–4½ Pounds (30 Infants) | 4½–5½ Pounds (62 Infants) |
|---|---|---|---|
| Foetal distress | 7 (44 per cent) | 8 (27 per cent) | 16 (26 per cent) |
| Asphyxia .. | 11 (69 per cent) | 15 (50 per cent) | 20 (32 per cent) |

### (b) *Postmaturity*

In 112 cases delivery occurred 14 days or more after the expected date of confinement. The weights of the children so born varied between 4 pounds 14 ounces and 11 pounds 13 ounces, the average being 7 pounds 12 ounces.

Table IV
*The Incidence of Foetal Distress and Asphyxia at Birth in Premature, Mature and Postmature Infants*

| | Cases | Foetal Distress (Per cent) | Asphyxia (Per cent) |
|---|---|---|---|
| Premature .. | 108 | 28·7 | 42·6 |
| Mature .. | 785 | 28·5 | 20·1 |
| Postmature .. | 112 | 39·3 | 30·4 |

Foetal distress was more frequently encountered in the postmature than in the premature group, but though the incidence of asphyxia was significantly raised when compared with the rate for mature babies, it did not reach the level found in the premature group. The greater part of this increase is probably related to the higher proportion of deliveries under general anaesthesia amongst postmature infants.

## IV. Hypertension, Pre-eclampsia and Eclampsia

In this series of 166 patients there are included 29 cases of hypertension, 135 cases of pre-eclampsia and 2 cases of eclampsia.

Foetal distress was apparent in 30·1 per cent of cases, a figure comparable with that for the whole series, and the incidence of asphyxia at birth, 28·3 per cent, is only slightly higher than 24·4 per cent for all babies. The exclusion of some of the more severe cases at an early stage of pregnancy by the liberal use of Caesarean section may have affected these figures.

## V. Ante-partum Haemorrhage

The numbers in this group are small as many cases of severe accidental haemorrhage resulting in immediate foetal death are excluded, as are also major types of placenta praevia necessitating Caesarean section. In the 26 cases that remain, foetal distress was noticed in 12 (46·1

per cent), and of the babies 9 (34·6 per cent) showed asphyxia, both figures being greater than those for the series as a whole.

## VI. Influence of Labour

### (a) *Normal Labour*

Patients delivered within 24 hours of the onset of labour, whether primiparae or multiparae, were considered to have had a normal labour, with the exception of a few patients in whom the second stage was unduly rapid.

In this group of 812 patients the incidence of foetal distress was 28 per cent and of asphyxia at birth 22·4 per cent.

### (b) *Long Labour*

With increasing length of labour the incidence of both foetal distress and asphyxia at birth mounts steadily.

Table V

*The Incidence of Foetal Distress and Asphyxia at Birth in Normal and Prolonged Labour*

| Duration of Labour | No. of Cases | Foetal Distress (Per cent) | Asphyxia (Per cent) |
|---|---|---|---|
| Under 24 hours .. | 812 | 28 | 22·4 |
| 24–47 hours .. | 129 | 38 | 27 |
| Over 48 hours .. | 34 | 55·9 | 53 |

### (c) *Prolonged Rupture of Membranes*

In 88 cases membranes were ruptured for longer than 24 hours. This was frequently performed as a surgical induction of labour because of some factor which in itself might adversely affect the child. The incidence of both foetal distress (34·4 per cent) and asphyxia at birth (36·3 per cent) was raised.

### (d) *Precipitate Labour*

The influence of very rapid labour on the frequency of asphyxia at birth was considered with special reference to the speed with which the second stage of labour was accomplished. For this purpose a labour in which the second stage lasted 5 minutes or less was considered to be precipitate. (Table VI.)

The numbers are small, but an extension of the definition to include cases in which the second stage lasted 10 minutes or less showed that the incidence of asphyxia was similar to that for the series as a whole.

Table VI

*The Incidence of Foetal Distress and Neonatal Asphyxia in Long Labour, Precipitate Labour and Normal Labour*

| | No. of Cases | Foetal Distress (Per cent) | Asphyxia (Per cent) |
|---|---|---|---|
| Long labour .. .. | 163 | 41·7 | 32 |
| Precipitate labour .. | 13 | — | 46 |
| Normal labour .. | 812 | 28 | 22·4 |

## VII. Pitocin and Morphia

(*a*) Pitocin was used to induce or expedite labour in 46 cases either by slow transfusion or by intermittent injection of 2 units. Foetal distress occurred in 14 instances (30·4 per cent) and 18 of the 43 liveborn infants (41·8 per cent) showed asphyxia at birth. The 3 stillbirths were associated in 2 instances with accidental haemorrhage, and in 1 with intracranial haemorrhage, but these cases are difficult to assess as in so many multiple adverse factors were present.

(*b*) Morphia was administered to the mother within the last 4 hours of labour in only 30 cases. Asphyxia was noticed in 14 babies (46·4 per cent), and, in a considerable number of these, delay in breathing was followed by evidence of respiratory depression without other signs of disease. N-Allyl-Normorphine was not in use in the early part of this investigation.

## VIII. The Maternal State

During the progress of the study it became apparent that a deteriorating maternal condition was often reflected in the foetus. Such deterioration is not readily measured, but a rise in the maternal pulse to 110 beats per minute or more was taken as an indication of maternal distress brought about by several causes including prolonged labour, heart failure and severe pre-eclampsia. In some instances these causes led to immediate operative delivery, but in others analgesics, intravenous fluids and oxygen not only improved the maternal state but appeared to lessen the signs of foetal distress.

The maternal pulse rose to 110 or more in 73 patients with signs of foetal distress in 37 (50·6 per cent). There were 3 stillbirths, 2 with preceding evidence of foetal distress and 1 without warning, and 53 per cent of the 70 liveborn infants showed asphyxia at birth.

### IX. Operative Delivery

Foetal distress is often the indication for speeding delivery by Caesarean section, or, after full dilatation of the cervix, by the application of forceps, but the operative delivery or the anaesthetic may in itself contribute to the asphyxia of the newborn child.

Table VII
*The Incidence of Foetal Distress and Asphyxia at Birth in Relation to Operative Delivery*

| | No. of Cases | Foetal Distress (Per cent) | Asphyxia (Per cent) |
|---|---|---|---|
| Forceps (local analgesia) .. | 22 | 50 | 31 |
| Caesarean section (general anaesthesia) | 36 | 52·7 | 47·1 |
| Forceps (general anaesthesia) | 105 | 51·4 | 66·7 |

Delivery was by forceps or Caesarean section in 163 cases. In slightly over half the cases there was already evidence of foetal distress, but, where it was possible to deliver by low forceps with local infiltration of the perineum, the incidence of asphyxia was only slightly raised (to 31 per cent). If there was no foetal distress preceding the application of forceps under local analgesia, no increase in neonatal asphyxia was found.

Table VIII
*Influence of Foetal Distress in Labour on Asphyxia in Babies Born by Operative Delivery*

| | Incidence of Asphyxia (Per cent) | |
|---|---|---|
| | No. Preceding Foetal Distress | Born After Foetal Distress |
| Forceps (local analgesia) .. | 18·1 | 45·4 |
| Caesarean section (general anaesthesia) | 35·3 | 57·0 |
| Forceps (general anaesthesia) | 62·7 | 66·6 |

Tables VII and VIII confirm the opinion that general anaesthesia is a factor in producing neonatal asphyxia.

The incidence of foetal distress in breech presentations was low (22·7 per cent), perhaps because meconium was accepted as a normal feature, but asphyxia at birth was present in 77·2 per cent of babies.

### X. Placenta and Cord Complications

(*a*) A number of placental abnormalities were discovered, and the conditions that were considered likely to affect the child in labour included small placentae weighing under 1 pound, circumvallate placentae, infarction involving one-quarter or more of the placenta, and retro-placental blood clot.

There were 70 such cases, foetal distress was encountered in 38·5 per cent and there were 6 stillbirths. Of the children born alive 43·7 per cent showed asphyxia at birth and 2 died later.

(*b*) In 24 cases there were cord complications, including true and occult prolapse of the cord, a short cord, a true knot and the cord tightly round the neck (17 cases). There were 12 instances of foetal distress and 12 of asphyxia at birth.

### XI. Stillbirths and Neonatal Deaths

(*a*) In the 12 cases of foetal death in labour, 5 occurred without warning. These 5 stillbirths were associated with prolonged labour; the cord was round the neck in 1 case, pre-eclampsia and placental infarction in another, 2 patients were postmature, and the fifth had no associated factor.

Of the remaining 7 stillbirths in which signs of foetal distress had been noticed, meconium was present in all but one. Contributing conditions included prolonged labour (2 cases), antepartum haemorrhage (2 cases), eclampsia and postmaturity (1 case of each), and in 1 no cause could be found.

(*b*) There were 23 deaths in the first 12 days of life: foetal distress had been noticed in 13 instances, and 20 (87 per cent) of the babies showed asphyxia at birth. Death was due to intracranial haemorrhage (5 cases), respiratory failure in the first 36 hours including atelectasis

and hyaline membrane (10 cases), congenital abnormalities (5 cases), 2 cases of infection and 1 of haemolytic disease.

## Discussion

Consecutive cases of patients in labour have been reviewed in an attempt to assess the significance of the recognized signs of foetal distress, so that guidance in the management of labour and urgency of delivery might be gained. Neonatal asphyxia is not often defined, but it was found that regular respiration was usually established within 1 minute of birth, and this formed a reliable indication of the child's state.

A rise in foetal heart rate to 160 or a fall below 100 beats per minute were seen to be of equal significance, and a fluctuating rhythm, though often associated with other signs of foetal distress, indicated an increase in the threat to the child. These findings do not quite bear out FitzGerald and McFarlane's (1955) statement that a rise in rate is more serious than a fall, and they are at variance with the general view expressed by the Editor of *Obstetrical and Gynecological Survey* (1955) that a fall in foetal heart rate is of greater significance. Moreover, Lund's (1940, 1943) statement that transient tachycardia is present in 17·6 per cent of cases and bears no relation to asphyxia at birth, could not be supported.

Whatever the signs of foetal distress may be, the risk to the child of asphyxia at birth was found to be considerably increased, and of all the single factors the passage of meconium gave the worst prognosis for the child. This is in agreement with FitzGerald and McFarlane's results, yet it is widely held that if the foetal heart is of normal rate and rhythm, the passage of meconium is inconsequential (*Obstetrical and Gynecological Survey*, 1955).

The serious significance of the major foetal heart changes is well recognized, but if these are awaited the opportunity for active intervention may already have been lost. For this reason the lesser deviations in foetal heart rate from a sustained level must also be considered in determining treatment, as they too carry a significant increase in the incidence of asphyxia at birth.

There are many factors which can be shown to have a direct bearing on foetal distress in labour, and asphyxia of the child at birth. FitzGerald and McFarlane could find no significant difference in the incidence of foetal distress in the various age groups, but contrary statements are made that the stillbirth and neonatal death rates rise in direct relation to increasing age. In the present series, age appeared to affect the issue only in so far as it could be associated with parity. Thus primiparity was linked with the highest incidence of foetal distress and asphyxia, the neonatal asphyxia again becoming prominent after the seventh child.

Foetal distress and particularly the state of the child at birth bore close relation to the weight, those babies under 4½ pounds showing significant variations in these two factors. Again in the postmature infant there was an increase in the incidence of foetal distress and asphyxia, findings that confirm earlier statements by McKiddie (1949) and Clayton (1953).

As might be expected, both long labour and prolonged rupture of membranes affected the child's condition not only *in utero* but also at birth, but sometimes maternal exhaustion from such diverse conditions as severe pre-eclampsia or a heart lesion was reflected in the alterations in foetal heart rate, and treatment directed to improve the maternal state resulted also in improvement in the foetus.

Operative delivery became necessary for a variety of reasons including foetal distress, and the results underline the significance of the general anaesthetic in its effect on the foetus. Where it was possible to deliver by forceps under local infiltration of the perineum, the risk of asphyxia was not increased, yet inevitably a general anaesthetic must be given for the more difficult deliveries, and in two-thirds of these cases asphyxia at birth can be expected to occur.

In the whole series 35 children died in the neonatal period or were stillborn. Perhaps by meticulous observation of the lesser variations in foetal heart rate and by earlier intervention, some of these lives might have been saved.

We would like to thank Professor Claye and Professor Craig for their assistance in the preparation of this paper.

## References

Clayton, S. G. (1953): *Proc. R. Soc. Med.*, **46**, 91.

FitzGerald, T. B., and McFarlane, C. N. (1955): *Brit. med. J.*, **2**, 358.

Lund, C. J. (1940): *Amer. J. Obstet. Gynec.*, **40**, 946.

Lund, C. J. (1943): *Amer. J. Obstet. Gynec.*, **45**, 636.

McKiddie, J. M. (1949): *J. Obstet. Gynaec. Brit. Emp.*, **56**, 386.

*Obstetrical and Gynecological Survey* (1955), **10**, 856.

von Winckel, F. (1903): *Handbuch der Geburtshülfe*. Bergmann, Wiesbaden.

# FORMATION OF AN ARTIFICIAL VAGINA BY FRANK'S METHOD

BY

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IN 1938 R. T. Frank of New York described a method of treating cases of congenital absence of the vagina by pressure to form an artificial vagina. He had been impressed during operations on these cases by the tenuous nature of the tissues separating rectum from bladder and urethra, and found that intermittent pressure could rapidly form a vagina, and he reported success in 5 cases out of 6. In 1940 he described some modifications in the details of his technique, reported a total of 9 cases, including a follow-up of some of the previous cases, and recommended that this method should entirely replace operation. This simple method was used with success in the following case.

## CASE REPORT

The patient was first seen at the age of 18 with primary amenorrhoea. Examination under anaesthesia showed the vagina to be absent, although two small pits were present. There was no evidence of a functioning uterus. Otherwise the patient was quite feminine, attractive and intelligent.

A year later, as she wished to get married and as her fiancé understood the position, the possibility of forming a vagina by Frank's method was discussed with her. The patient agreed to try the method, especially as she wished to continue working. She was therefore provided with a plastic rod, $\frac{5}{16}$ inches in diameter, and was instructed to press this downwards and backwards once or twice a day. A month later there was a small depression, and 4 months later there was a depression 1 inch (2·5 cm.) deep. A second rod $\frac{1}{2}$ inch in diameter was provided, and she was instructed to continue pressure in the axis of the normal vagina. Later a shorter instrument $\frac{3}{4}$ inch in diameter with a flange was given to her and she was instructed to wear this at night. Seventeen months after treatment had been started she was married, and the vagina was then $1\frac{1}{2}$ inches (4 cm.) deep.

Recently the patient, who is now 25, and her husband, who is 27, have been interviewed after over 4 years of married life. They are both happy, and intercourse takes place regularly and is fairly satisfactory. The vagina admits a small dilator, but is somewhat deficient in length, being only 2 inches (5 cm.) long.

## DISCUSSION

The use of pressure to form an artificial vagina in these cases is probably the oldest of all methods, as cases have occurred from time to time in which the efforts of the husband have achieved this end. Frank's method avoids operation and admission to hospital, but requires some intelligence and perseverance on the part of the patient. In addition to Frank's cases others have been described by Holmes and Williams (1940), Campbell (1941), Brady (1945) and Dawson (1945) in which it was successful.

The formidable operations once described for the treatment of this condition have now become of historical interest, and the only operative procedure which seems to find general acceptance in this country and America is that in which a space is dissected up between bladder and rectum into which a skin graft is inserted upon a mould. This has been developed by McIndoe (1950), who reported 50 excellent results in 63 cases, and Counseller (1948), using McIndoe's technique, with 55 good results in 70 cases. It would seem, therefore, at the present day that the choice of treatment must lie between the method of Frank and the operation advocated by McIndoe. This operation is a major one needing prolonged after-treatment and

carrying some risk of fistula formation. It has, however, the great advantage that a vagina of adequate length is formed, and McIndoe found that in 50 out of 63 cases the length of the vagina was 4½ inches (12 cm.). Counseller says that Frank's method would be the ideal one "if sufficient depth could be obtained in all cases", and McIndoe criticizes it on the ground that "while the perineum is of considerable elasticity it is unlikely to yield to the desired extent with uniformly good results". It does appear that with Frank's method the vagina remains limited in length, and in 12 reported cases in which the length was given I have found that in none was a greater length than 3½ inches (9 cm.) obtained, and in 7 of these it was less than 2⅞ inches (7·5 cm.). In all of the cases in which coitus took place, however, it was described as being satisfactory, and it would appear therefore that this deficiency in length is not a serious disadvantage of the method. There also appears to be, according to Frank's figures, some increase in length after marriage.

A great advantage of Frank's method is that a vagina of some length can be made in a very short time, and Frank stressed the importance of the initial stages of the treatment being carried out quickly. Although in the case described above the treatment lasted over 17 months, in 4 of the other cases reported in the literature an adequate vagina was formed in 8 weeks or less, and in another case the patient was married less than 13 weeks after the start of treatment. In Dawson's case a vagina of 2 inches was made in 10 days "with surprising ease and without pain".

Frank says that his procedure is "so simple, so effective and the result so uniformly successful that it should entirely supersede operative measures". His conclusions were based on an experience of 30 cases of this uncommon condition, and his name moreover had previously been associated with an operation for it. The usefulness of this method does not appear to be widely known, and the experience of this single case supports the view that at least the alternative treatments should be discussed with the patient.

## Summary

A case of congenital absence of the vagina treated by the non-operative method of Frank is described, and the advantages of this simple method are discussed.

## References

Brady, L. (1945): *Ann. Surg.*, **121**, 518.
Campbell, K. (1941): *Med. J. Aust.*, **2**, 650.
Counseller, V. S. (1948): *J. Amer. med. Ass.*, **136**, 861.
Dawson, J. B. (1945): *N.Z. med. J.*, **44**, 132.
Frank, R. T. (1938): *Amer. J. Obstet. Gynec.*, **35**, 1053.
Frank, R. T. (1940): *N.Y. St. J. Med.*, **40**, 1669.
Holmes, W. R., and Williams, G. A. (1940): *Amer. J. Obstet. Gynec.*, **39**, 145.
McIndoe, A. (1950): *Brit. J. plast. Surg.*, **2**, 254.

# PREGNANCY IN THE DEFORMED UTERUS

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DURING the past fifteen years I have had the good fortune to see or to study the records of 65 patients with proved major uterine deformity and many with minor deformity. Thanks to the co-operation of my colleagues I have been able to examine most of these patients. My remarks will be based primarily upon a study of the records of pregnancies in 38 cases of true double uterus from this series with a detailed obstetrical history available, upon my personal experience of the supervision of many of these patients during one or more of their pregnancies or labours and upon a survey of the literature.

I define double uterus as a uterus derived from only one pair of Müllerian ducts, and therefore having only one pair of tubes, with two separate cavities which do not communicate with one another above the level of the internal cervical os. I suggest that, to avoid ambiguity, the descriptive term for uterine deformity should, whenever practicable, convey information regarding the external conformation of the uterus, particularly of the uterine fundus, the type of uterine cavity, particularly whether it is single or double, and the type of cervix, particularly whether there are one or two cervical canals. The principle can readily be applied to those cases in which the errors of development are due to failure of approximation and fusion of the Müllerian ducts but it is not so readily applied to those in which deformity is due to partial or complete failure of development of the Müllerian system (Hunter, 1950).

## FERTILITY

Conflicting opinions are given regarding the fertility of patients with errors of fusion of the Müllerian ducts. Of my 51 patients with true double uterus 38 were married women. One of these patients had been married for only three months and an unmarried patient recently had her third Caesarean section at the age of 21 years. In this series were included all patients with proved double uterus whose records were reasonably complete. The forms now in use have been used to supplement but not to replace the ordinary hospital or private records to ensure that detailed accounts are available for reference.

My control cases were taken from hospital records, each control being paired with a double uterus case of the same age group (i.e., age $\pm$ 2 years). Controls for cases of double uterus first seen as gynaecological cases were taken from gynaecological records and as obstetrical cases from obstetrical records. All controls for married patients were married and for single patients were unmarried.

In my series (Table I) of 38 married women with proved double uterus fewer patients had been pregnant and they had had fewer total pregnancies and fewer viable pregnancies than those in the control series. More of those patients with uterine deformity had had no pregnancies. On the other hand, of the 28 married women who had been pregnant more had been pregnant and approximately the same number had had viable pregnancies as those in the control series. These figures indicate that, although five times as many patients with double uterus fail to fall pregnant as in the control series, patients with double uterus who have overcome the difficulty of falling pregnant for the first time are no longer infertile.

TABLE I
*38 Married Women with Confirmed Double Uterus*

| | Double Uterus | Control |
|---|---|---|
| Total married women .. .. .. | 38 | 38 |
| Fertile women .. .. .. | 28 | 36 |
| Total Married Women .. .. | 38 | 38 |
| No. of pregnancies .. .. .. | 70 | 83 |
| Viable pregnancies .. .. .. | 55 | 73 |
| Non-viable pregnancies .. .. | 15 | 10 |
| Fertile Women .. .. .. .. | 28 | 28 |
| No. of pregnancies .. .. .. | 70 | 64 |
| Viable pregnancies .. .. .. | 55 | 56 |
| Non-viable pregnancies .. .. | 15 | 8 |

Infertility may sometimes be due to unsatisfactory intercourse or to failure of access of spermatozoa to the horn in which the expectation of a successful pregnancy is greater when the vagina is septate. In a series of pregnancies, successive pregnancies may occur in the same horn or, probably less commonly, they may alternate in the two sides of the uterus.

When dyspareunia is due to the presence of a septum narrowing the vaginal canal, longitudinal division of the septum under general anaesthesia may be necessary. As thick septa can be very vascular bleeding points should be carefully ligated. The septum should not be crushed by clamps or cauterized to control haemorrhage in case this should cause fibrosis and distortion of the vagina leading to further dyspareunia and, possibly, to difficult labour.

A septum, even when thin, may also be divided in cases of infertility to facilitate access of spermatozoa to both cervices and uterine cavities at each coitus and so to improve the chances of conception. The expectation of successful pregnancy may be greater in one horn, usually the better developed horn, than in the other in a case of double uterus and the improved development resulting from a pregnancy, even if this ends in abortion, probably increases the prospects of a patient falling pregnant again and of that pregnancy being carried to a successful termination.

### TWINS

There is said to be a high incidence of twin pregnancy in double uteri. Berkeley, Bonney and MacLeod (1938) state that this is as high as 1 in 12 pregnancies compared with 1 in 69 in single uteri. I have not personally seen a case of twin pregnancy and no case has occurred in my series, but the occurrence of twins in double uterus has been recognized for many years. Brown (1956) gives an excellent demonstration of the radiographic findings in such a case. The foetal heads lie at the same level, as in conjoined twins, but the foetal trunks diverge and lie in the mother's flanks. One twin occupies each horn of a uterus bicornis bicorpus bicollis. When both foetuses occupy the same uterine horn the pregnant horn is usually inclined to one side of the abdomen but, in view of the bulk of its contents, it is not necessarily confined to one side in advanced pregnancy.

Ross (1871) reported a case of miscarriage of twins at 5-months pregnancy followed fifteen weeks later by the delivery of a healthy mature child. The mother had previously given birth to 6 living children, and, apart from the fact that one child had been premature, nothing unusual had been noticed in the pregnancies or labours.

Stabler (1955) had a patient who was admitted to hospital as a case of intra-uterine foetal death at 12-months pregnancy. No movements had been felt for 5 months and the uterine size corresponded with a pregnancy at term. After failed medical induction the patient was sent home. Two years later, 6 months after the normal delivery of a living child at home, Farquhar Murray delivered a grossly macerated foetus by Caesarean section and performed hemi-hysterectomy for double uterus. The patient had been pregnant for 3 years and had had a normal pregnancy in one horn while a macerated foetus lay in the other horn.

Bainbridge (1924), who quoted several examples of super-foetation and superfecundation, stated that Jellinghaus had described a case of pregnancy at term in one with a 4-months foetus in the other horn and a patient who, 2 months after having been delivered of a mature white baby from the left horn of a double uterus, had given birth to a mature black baby from the right horn.

### ABORTION

In all cases of uterine anomaly the abortion and miscarriage rate is high and repeated

abortions are not uncommon. Miller (1923) found that only 42 per cent of patients had normal spontaneous delivery at term. The risk of abortion is probably greatest in patients with major uterine deformity especially when the fundal recess of the pregnant horn is constricted as in many cases of bicornuate uterus, whether or not the cavity is divided as far as the internal cervical os. It is least when the conformation of the cavity approximates to normal. In some cases abortion may be more liable to occur when the pregnancy is in one and less liable to occur when in the other horn. The aborting horn may show imperfect development but this is not usual. The risk of miscarriage may also be greater when the placenta is attached to a uterine septum. Abortion may be accompanied by haemorrhage which is sometimes very severe and difficult to control.

In my series of cases of double uterus (Table I) 39 per cent of patients who had fallen pregnant had had at least one abortion or miscarriage and 21 per cent of all pregnancies had terminated before the 28th week compared with 29 per cent and 16 per cent in the control series.

If evacuation of the uterine contents is necessary for inevitable or incomplete abortion a careful examination should be made to ensure that the pregnant horn is, in fact, being curetted. It may be helpful to remember that the non-pregnant horn may occasionally be erect and the pregnant horn may lie beside or behind it. The medial walls of a dichotomous uterus may be thin and susceptible to damage by the dilators.

Mosher (1924) recounted the story of a case in which a professional abortionist had punctured the non-pregnant horn of a double uterus, presumably leaving the pregnant horn undisturbed. The patient died from general peritonitis.

From time to time various operations designed to unite the cavities of a double uterus, such as Strassmann's metraplasty, have been recommended but I think that the indications for such operations are few.

### Extra-Genital Deformity

The possible co-existence of extra-genital deformities with abnormalities of the genital tract has long been recognized. These may assume major importance during pregnancy especially as those most frequently encountered are abnormalities of the urinary tract which may, in some cases, be associated with impairment of renal function. Cases of absent kidney, pelvic horse-shoe kidney and other renal abnormalities have been described and may be of serious import. Other deformities such as double ureter, double bladder and ectopia vesicae may co-exist with uterine deformities. It is important that such abnormalities should be recognized at the earliest possible date, preferably in the non-pregnant state if major disasters are to be avoided. The renal tracts of all patients with known uterine deformities should therefore be fully investigated without delay, if possible before or between pregnancies.

The patient with a double uterus is also subject to any of the complications of pregnancy which can affect the woman with a normal uterus. Uterine fibroids, without or with early pregnancy, may simulate double uterus or other uterine malformation and uterine deformities may be mistaken for fibroids. Even in advanced pregnancy it may be difficult to differentiate between a non-pregnant uterine horn and a posterior cervical fibroid or between a fundal deformity and a soft fundal interstitial fibroid.

### Nature of Deformity

During pregnancy even in the absence of fibroids it may be difficult or impossible to decide the precise nature of a uterine deformity. A broad fundus with a depression, indentation or groove at or near the centre may indicate the presence of an arcuate, cordiform, sub-septate or septate uterus. On the other hand a similar appearance may be found in sacculation of the uterine fundus, usually near a cornu, with the foetal head in breech presentation or oblique or transverse lie or, less commonly, with the breech in cases of vertex presentation or oblique or transverse lie. In some cases of transverse lie both the head and breech may elevate and pouch the uterine fundus near the cornua.

In cases of cordiform and simple septate uterus fundal deformity is often accentuated by the resistance to expansion of the myometrium at the site of imperfect union, usually apparent at

the fundus, as the uterus enlarges. The deformity becomes more apparent as the enlargement of the non-pregnant horn lags behind that of the pregnant horn with advancing pregnancy. An asymmetrical uterus with a notched outline may result from the more rapid enlargement of the pregnant side of the simple septate or cordiform uterus than of the non-pregnant side with accentuation of the line of partition. On the other hand it may be due to the elevation of the point of union of the two horns of a bicornuate uterus cleft to a level above that of the internal os. If the cleft extends to or through the internal os the non-pregnant horn remains in the pelvic cavity. An accurate diagnosis of the precise nature of the deformity can be made only some time after delivery and possibly, then, only after a hysterogram has been taken. The importance of making an accurate diagnosis of cases of uterine deformity, whether suspected or positively diagnosed, in the non-pregnant state is apparent.

During the course of a Caesarean section upon a uterus cordiformis sub-septus I have, on one occasion, seen a fundal loculus on one side shielded by the laterally displaced septum and bridged by the foetal membranes. The foetus was presenting by the vertex and twin pregnancy was not found. On separating the membranes after delivery one or two ounces of clear fluid escaped from the loculus in the left cornu which had a smooth wall and no readily detachable lining. I concluded that this must be a fundal recess of a subseptate uterus lined by decidua which had not been reached by the chorion.

### Myometrium of Pregnant Horn

In an arcuate uterus the centre of the fundus and in a bicornuate uterus the medial border of the pregnant horn may be thin (Macdonald, 1949). This may be apparent when manual removal of the placenta is necessary, especially when the placenta is implanted upon the thin area. It may be associated with diminished vascularity of the myometrium, and placental insufficiency, foetal anoxia and foetal distress or even intra-uterine foetal death may occur before or during labour when the placental site overlies one of these parts. Non-detachment and retention of the placenta is common in cases of uterine deformity, and although I have not seen a case recorded, it is not improbable that the thin uterine wall may be torn during manual removal of a non-separated retained placenta. Even curettage for abortion does not seem to be free from risk of perforating the wall of a bicornuate uterus as the horns are commonly directed towards the lateral pelvic walls rendering the superomedial walls of the uterus even more vulnerable.

In the double uterus the pregnant horn is often fusiform and the lower segment may be small, funnel-shaped and indistensible in contrast to the normal lower segment of a uterus with minor deformity. A tapering lower segment may hinder descent of the presenting part in late pregnancy, favour the occurrence of frank breech presentation and predispose to disordered uterine action during labour. In cases of major uterine deformity the pregnant uterus is usually asymmetrical and commonly deviates to one side of the abdomen.

### Presentation

The disposition of the foetal parts in a deformed uterus is of great importance. When the vertex presents in a case of double uterus the head, in advanced pregnancy, is usually very well flexed and may show moulding even when lying above the pelvic brim. It is commonly at a high level and may be displaced towards the side of the abdomen on which the back lies. It may be difficult or impossible to fit it into the pelvic brim. The foetal trunk may be displaced laterally and may be lying obliquely in the flank. The foetal back may lie either towards the mother's flank or towards the medial aspect of the pregnant horn and the legs are usually closely applied to the ventral aspect of the foetus.

Breech presentation is common in cases of double uterus. In my series (Table II) there were

Table II
*Breech Presentation*

| | Double Uterus | Control |
|---|---|---|
| Total fertile women .. .. | 28 | 28 |
| Patients with breech presentation | 10 | 1 (twin) |
| Total viable pregnancies .. .. | 55 | 56 |
| Breech presentations .. .. | 14 | 1 (twin) |

14 breech deliveries in 55 viable pregnancies, The legs are nearly always extended and closely applied to the foetal abdomen and thorax. The foetus on palpation or X-ray seems to be long and tapering and the head, lying in the fundus, may sometimes show moulding. Although the breech may not be deeply engaged in the pelvis it is difficult to disengage and external version is seldom possible. The pregnant uterine horn and foetus are commonly lying to the side of the abdomen.

In about 1 in every 9 cases of transverse lie the uterus is abnormal and nearly always has a single deformed cavity. The foetal back lies across the pelvic brim more often than across the fundus. Breech presentation is also relatively common in such cases and twin pregnancy, which may be even more than usually difficult to diagnose, must not be overlooked.

### Non-pregnant Horn

Let me turn again to the non-pregnant side of the uterus. If the cleft in a bicornuate uterus does not reach the level of the internal os, the hypertrophied non-pregnant horn is lifted by its rising attachment to the pregnant horn to a higher level as pregnancy progresses.

If the uterus is dichotomous, with the cleft extending down to or through the internal os, it will almost invariably remain in the pelvic cavity and may rotate posteriorly into the pouch of Douglas. It may there enlarge and obstruct the advance of the foetus during labour. It must then be differentiated particularly from posterior cervical fibroid, ovarian cyst and twin pregnancy with double vertex presentation. During labour, and occasionally before the onset of labour, palpable contractions of the non-pregnant horn may be observed and may assist the differential diagnosis from other pelvic tumours (Robinson, 1946).

When posterior rotation of the non-pregnant horn takes place it may be accompanied by axial rotation of the uterus. The broad ligament related to the pregnant horn may then be carried forwards towards the mid-line and the anterior abdominal wall. This may add to the technical difficulties of Caesarean section as the vascular broad ligament commonly presents in the abdominal wound.

Herd (1945) reported a case of torsion of the pregnant horn associated with symptoms and signs suggesting the occurrence of concealed accidental haemorrhage and Horn (1924) and Caswell (1926) described a case of torsion at 6-months pregnancy followed by the breech delivery of a living child two years later. In both cases the gangrenous pregnant horn was removed by subtotal hemi-hysterectomy.

In one of my patients minor dextro-rotation of the uterus with anterior sacculation of the lower part of the pregnant left horn was accompanied by rotation of the non-pregnant horn into the pouch of Douglas. This caused an oblique lie with the presenting head lying in the left uterine cavity in the right iliac fossa while the breech occupied the left cornu in the left hypochondrium. In this case the left broad ligament did not present in the abdominal wound.

Decidual change takes place in the non-pregnant horn and an intermittent discharge of clear fluid may occur during pregnancy. Although amenorrhoea is the rule, the non-pregnant horn may occasionally discharge blood of menstrual type, sometimes at monthly intervals, during the whole or part of pregnancy. This may give rise to a mistaken diagnosis of threatened abortion or true ante-partum haemorrhage. In cases of doubt it is safer to assume that these complications are present until it is proved otherwise. A decidual cast, complete or fragmented, may be discharged from the non-pregnant horn before, during or after labour.

### Cervix

The cervix of a deformed uterus may be single, with a single canal, or double, with two canals. The double cervix may have a septate canal or diverging cervices, as in uterus pseudo-didelphys, or separate, almost parallel, canals with separate cervices, as in uterus didelphys. In some cases the cervix of the non-pregnant horn may be forced down in advance of the presenting part and may even appear at the vulva. This usually indicates that the non-pregnant horn of the uterus is lying below the presenting part and may obstruct labour. Occasionally partial dilatation of the cervix of the non-pregnant uterus may occur during labour. If this cervix is low it may be mistaken for the cervix of the pregnant horn.

A cervical septum may tear or obstruct the advance of the foetal head (Arthur, 1948) or a uterine septum may tear above the level of the internal os and the leading part of the foetus may present at the non-pregnant cervix. A vaginal septum may also delay the advance of the foetus through the narrow vaginal canal. It will usually tear and the laceration is liable to occur in the groove between the septum and the anterior vaginal wall where there is a risk of injury to the bladder. Free haemorrhage may occur from the torn septum. Occasionally a vaginal septum may obstruct labour.

A recto-vesical septum dividing the pouch of Douglas into two compartments is almost invariably present in cases of dichotomous uterus. Its presence may add to the difficulty of bladder reflexion for lower segment Caesarean section and troublesome haemorrhage may occur from its blood vessels. Care must be taken to avoid injury to the bladder during stripping.

## Pregnancy

In many cases pregnancy is normal in every respect but patients with uterine deformity are subject to the same complications of pregnancy as those with normal uteri. The incidence of unavoidable haemorrhage, cephalo-pelvic disproportion and medical and surgical disorders is probably the same in both groups of cases. It has been said, however, that there is an increased risk of hyperemesis, toxaemia and accidental haemorrhage in cases of major deformity. Intermittent bleeding from the non-gravid horn may occur especially in the early months, but this is not usual. The abortion rate is high, miscarriages are common, premature labour is liable to occur and even babies born at term may be smaller than average. Fenton and Singh (1952) found the viable birth rate only 66·4 per cent compared with the "normal" rate of 93·1 per cent and the birth rate at term 56·1 per cent compared with the "normal" rate of 85 per cent in the Sloane Hospital in New York.

On rare occasions a pregnant horn in a single or a bicornual twin pregnancy may become impacted in the pouch of Douglas in early pregnancy. Uterus bicorpus is commonly associated with frank breech presentation and uterus unicorpus with a deformed cavity with shoulder, back or breech presentation. Placental insufficiency giving rise to foetal distress may occur when the placenta overlies the thinned medial border of a bicornuate or the fundus of an arcuate uterus even before the onset of labour. Intra- or extra-peritoneal haemorrhage can occur from thin-walled varices which may be seen in the broad ligament or on the posterior uterine wall. On rare occasions a decidual cast of the non-pregnant horn may be expelled in late pregnancy (Corbett, 1945) or during labour.

*Labour and Puerperium.* The onset of labour may be delayed in cases of double uterus for a week or more beyond the estimated date of confinement and may be preceded by low backache and intermittent abdominal discomfort for several days. This delay may cause anxiety because of the large size of the child and the risk of placental insufficiency. Labour, once started, may be slow in becoming established and may be prolonged by hypotonic inertia, hypertonic inco-ordinate uterine action or, in some cases, by retentive uterine hypertonus. This risk of disordered uterine action may be greater in cases of true double uterus with increased resistance to descent of the foetus due to a small, indistensible, funnel-shaped lower segment, a cervical or vaginal septum or a non-gravid semi-uterus lying in the pouch of Douglas. Contraction rings may develop and, particularly in cases of uterus unicorpus with transverse lie, early rupture of the membranes and prolapse of the cord or a limb may occur.

Tonic uterine contraction due to obstructed labour and leading to lower segment uterine rupture is unusual but rupture of the thinned wall of an arcuate or bicornuate uterus or of a Caesarean, myomectomy, hemihysterectomy or metraplasty scar may take place especially in the presence of transverse lie or obstructing non-pregnant body (Lyle, 1904). It seems that rupture of the lower segment is a commoner complication of vertex than of breech presentation.

The cervix of the non-pregnant horn of a double uterus may dilate to admit one or two fingers and, on rare occasions, the foetus may present at and descend through this cervix after laceration of a uterine or cervical septum. In

other cases the cervix of the non-gravid side may be forced down into the lower vagina in front of the presenting part and the attached horn will probably impede the further descent of the foetus. When each cavity of a double uterus holds a foetus the two uteri may contract independently and the cervices may dilate at different rates. Several hours or even days may elapse after the birth of the first baby before the second twin is delivered.

The risk to the foetus before and during labour is greater in cases of abnormal than of normal uteri and the stillbirth rate is correspondingly raised. There is also said to be an increased incidence of foetal deformity but I have not yet seen such a case.

In the third stage of labour retention of a non-separated or partially-separated placenta is common but morbid adhesion is unusual. The placenta is sometimes thin, extensive and irregular in outline. The risks of increased post-partum blood loss and of frank atonic post-partum haemorrhage are very real. The hazard may be greater when the uterus is not deeply cleft externally and the hypertrophied non-pregnant horn, raised into the abdomen and having an extensive attachment to the pregnant horn, may hinder uterine retraction during and after the third stage. If the placental site is on the uterine septum or a thin area of uterine wall control of bleeding from the torn sinuses may be less satisfactory in view of the inefficiency of the myometrium in those areas. In the majority of cases, however, there is partial detachment of a retained placenta or retention of placental fragments. Traumatic post-partum haemorrhage due to laceration of the vagina or of a cervical or vaginal septum may occur and an anterior vaginal laceration may involve the bladder wall. A few cases of acute inversion of the uterus have been reported in the literature.

The puerperium is usually uneventful but the blood loss may be in excess of normal and may continue for a longer period than is usual. Retention of placental fragments is not uncommon. On occasion free drainage of lochia from the recently pregnant horn may be hindered by the pressure of the subinvoluted second horn in the pouch of Douglas. A decidual cast may be passed from the non-pregnant horn in the early puerperium. This may be complete but is more often fragmented and in some cases the decidua may involute, organize and be largely retained. Expulsion of a cast is usually preceded and accompanied by intermittent backache and pelvic pain which may last several hours.

## Management

Close antenatal supervision of every patient with uterine deformity is essential. Bed rest in the afternoons and for two or three days each month at the time of the suppressed periods for the first 20 weeks and afternoon rest for the last 6 weeks are minimum requirements. Heavy housework and weight-lifting must be avoided and any blood loss or uterine colic, even when the presence of double uterus is known, must be treated by bed rest and sedation until it has been confirmed by speculum examination that no blood is escaping from the pregnant side of the uterus.

In the later months repeated careful clinical assessment supplemented, when necessary, by radiological examination is even more important than in normal cases. Information regarding the lie, presentation, position and disposition of the foetal parts and the relationship between the presenting part and the pelvic brim is indispensable and knowledge of the precise type and degree of uterine deformity acquired in the non-pregnant state is invaluable. The presence of cephalo-pelvic disproportion or disproportion between the foetus and birth canal must not be overlooked. The conformation of the uterus should be carefully observed as pregnancy progresses and, in cases of double cervix, it should be known before the onset of labour which cervical canal communicates with the pregnant uterine cavity. The approximation of the presenting part to the cervix and the presence or absence of dilation of the internal cervical os with consequent taking up of the cervix should be carefully noted. Malpresentation should be corrected when practicable, especially when the lie is transverse, but force must not be used and general anaesthesia is inadvisable for external version. Surgical induction of labour is not recommended in the presence of double uterus but may sometimes be of value, especially in the

multigravida nearing term, after correction of a recurrent malpresentation associated with relatively minor uterine deformity. Caesarean section, usually by the lower segment, is occasionally required either for foetal distress in late pregnancy or for one of the general indications such as disproportion or antepartum haemorrhage.

In all known cases of uterine deformity labour should be conducted in hospital. Careful and correct routine observation and management of normal and prolonged labour are essential. When labour is established, usually at about two-fingers cervical dilation, a vaginal septum should be completely divided as far as the vaginal vault under general anaesthesia and all bleeding points ligated under direct vision. I have never seen such an incision extend into the cervix. If the septum is left intact it may impede the descent of the presenting part, prevent expansion of the upper vagina, and, by reflex action, interfere with normal uterine function. It may lacerate and the tear may involve the anterior vaginal wall and even the bladder. Its presence may add to the risk of intra-cranial trauma and pressure necrosis of the foetal scalp and, in rare instances, it may cause obstructed labour. Likewise, a cervical septum may check the descent of the presenting part and cause obstructed labour or disordered uterine action and should then be divided. Disordered uterine action, malpresentation, obstructed labour and foetal or maternal distress should be treated according to general principles. Medio-lateral episiotomy should be used somewhat freely during vaginal delivery by natural forces, forceps or breech. Internal version should be avoided as far as possible and great care should be taken to avoid injury to the thin fundus of an arcuate or supero-medial wall of a bicornuate uterus should internal version prove essential. Caesarean section may be required in a fairly high proportion of cases, the indications being the same as in cases of normal uterus, but it should be borne in mind when dealing with young patients that if vaginal delivery has been possible in one pregnancy the myometrial development, lower segment expansion and cervical and vaginal dilatation all improve uterine efficiency and increase the chances of vaginal delivery in a subsequent pregnancy.

Bradley, Colozzi and Linthwaite (1954) stress the importance of routine examination of the pelvic organs during the course of any Caesarean section and this should be carried out during laparotomy for any purpose to ensure that pelvic abnormalities will not be overlooked.

Posterior rotation of the non-pregnant uterine horn into the pouch of Douglas may be associated with anterior rotation of the lateral wall of the pregnant horn and its vascular broad ligament may be carried forwards to present at the abdominal parietal incision and may be difficult to displace from the mid-line. It may then be necessary to extend the parietal incision to allow reasonable access to the lower segment without risk of damage to the broad ligament vessels. A transverse lower segment incision may threaten to extend laterally into the advanced broad ligament and cause severe haemorrhage.

The non-pregnant horn may be impacted in the pouch of Douglas and dislodgement from the pelvis to facilitate exposure of the anterior wall of the lower uterine segment may be difficult and may be attended by a certain risk of laceration of one of the enlarged broad ligament veins. I have never had the temerity to dislodge a non-pregnant obstructing horn and allow labour to proceed. This may avoid the need for uterine incision in a few patients but, in view of the high incidence of complications and the possibility of Caesarean section being necessary at a later stage of the same labour, I do not think the use of this procedure can be justified except in extraordinary circumstances. I have on one occasion seen a transverse incision in a narrow funnel-shaped lower uterine segment extend across the septal barrier into the cavity of the non-pregnant horn.

It is frequently advisable, before displacing the bladder downwards to expose the lower segment of a double bicornuate uterus, to divide the recto-vesical septum transversely as it crosses the uterine saddle while incising the utero-vesical pouch of peritoneum. This must be done with great care as the bladder may be closely approximated to the rectum over the uterus and may therefore be more than usually vulnerable. If this septum is not divided the

FIG. 1

Double uterus after Caesarean section showing small lower segment.

FIG. 2

Double uterus after Caesarean section showing posterior varices.

risk of bladder injury may sometimes be increased and recto-vesical vessels may be torn during the course of the operation.

If a small lower segment is too narrow for a transverse incision it is unlikely that a vertical incision will be adequate as the presenting part will probably be very high and the lower segment not expanded. Rather than extend the incision up into the junction between the upper and lower segments it is advisable to perform a deliberate upper segment operation with an anterior vertical incision.

In the absence of special indications such as degenerating fibroids or vascular complications I do not advocate removal of a non-pregnant horn obstructing labour as this may decrease fertility and increase the risk of uterine rupture in a later pregnancy.

After Caesarean delivery in a simple or cordiform septate uterus the advisability of dividing the exposed septum in a longitudinal direction in the lower uterine segment and cervical canal might be considered with a view to reducing the strain upon the lower segment Caesarean scar in a future pregnancy, increasing the capacity of the lower segment and facilitating expansion of the lower segment and descent of the presenting part in labour. The operation would be unsuitable for a deeply cleft uterus and the risks of haemorrhage from the divided septum and, later, of abortion would have to be taken into account. I personally believe that such an operation will seldom be advantageous.

The risk of intra- and post-partum haemorrhage after vaginal delivery must be minimized by the scrupulously correct management of the third stage of labour, the careful selection of cases and timing for manual removal of a retained placenta and the judicious use of ergometrine. Care should be taken to avoid tearing the thin areas of the uterine wall during digital separation of the placenta.

In conclusion I would like to stress that, when practicable, uterine deformities should be fully investigated in the non-pregnant state and that patients with known uterine deformity should always be delivered in hospital.

## References


Arthur, H. R. (1948): *J. Obstet. Gynaec. Brit. Emp.*, **55**, 766.

Bainbridge, W. S. (1924): *Amer. J. Obstet. Gynec.*, **7**, 285.

Berkeley, C., Bonney, V., and MacLeod, D. (1938): *The abnormal in obstetrics*. Arnold, London. p. 200.

Bradley, J. J., Colozzi, A. E., and Linthwaite, R. F. (1954): *Amer. J. Obstet. Gynec.*, **68**, 1174.

Brown, D. B. (1956): *J. Obstet. Gynaec. Brit. Emp.*, **63**, 395.

Caswell, C. C. (1926): *Amer. J. Obstet. Gynec.*, **11**, 853.

Corbett, R. M. (1945): *Trans. N. Engl. obstet. gynaec. Soc.*, p. 34.

Fenton, A. N., and Singh, B. P. (1952): *Amer. J. Obstet. Gynec.*, **63**, 744.

Herd, S. B. (1945): *Trans. N. Engl. obstet. gynaec. Soc.*, p. 36.

Horn, H. W. (1924): *Arch. Surg.*, **9**, 606.

Hunter, W. (1950): *J. Obstet. Gynaec. Brit. Emp.*, **57**, 721.

Lyle, R. P. R. (1904): *J. Obstet. Gynaec. Brit. Emp.*, **6**, 438.

Macdonald, C. R. (1949): *Trans. N. Engl. obstet. gynaec. Soc.*, p. 58.

Miller, N. J. (1923): *Amer. J. Obstet. Gynec.*, **4**, 398.

Mosher, G. C. (1924): *Amer. J. Obstet. Gynec.*, **7**, 322.

Robinson, T. G. (1946): *Trans. N. Engl. obstet. gynaec. Soc.*, p. 35.

Ross, J. H. (1871): *Lancet*, **2**, 188.

Stabler, F. E. (1955): Personal communication.

# A CASE OF UTERO-COLIC FISTULA DUE TO DIVERTICULITIS

BY

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FISTULA formation is a relatively common complication of diverticulitis; communication between the colon and each of the pelvic organs has been described. Nevertheless few cases of utero-colic fistula have been recorded, and diverticulitis as it affects the female pelvic organs is scarcely mentioned by many authorities on the subject.

Bacon (1949) discovered an incidence of uncomplicated diverticulosis of 7 per cent in a study of 2,747 consecutive barium enema investigations. From a series of 14,695 X-ray examinations of the colon, Ransom (1954) found that 1 in 8 patients had diverticula.

In a comprehensive review of the literature, Arnheim (1940) combined the results reported by many authors. These large numbers revealed that peridiverticulitis occurred in 20 per cent of 1,049 cases, fistula formation in 8 per cent of 1,516, abscess formation in 19 per cent, and peritonitis in 12 per cent of 834 cases of diverticulitis of the colon. That no mention is made of utero-colic fistula in any of these cases is an indication of the rarity of the condition. Fistula formation, like haemorrhage, obstruction, perifonitis and abscess formation demands surgical intervention; this being so, the rare cases of utero-colic fistula are not likely to be overlooked.

Ransom (1954) reported a case of utero-colic fistula associated with diverticulitis; Johnston and Stubbs (1955) likewise recorded a single case. Woodrow Cox (1952), in a paper discussing diverticulitis and the gynaecologist, described a case of salpingo-colic fistula and mentioned that utero-colic fistulae are much commoner. Whilst this may be so, the cases do not appear to have been recorded in any number.

## CASE REPORT

Mrs. E.M., aged 74 years, was first seen in the Gynaecological Department in October, 1955 complaining of an offensive vaginal discharge for 4 months, and slight vaginal bleeding for a few hours occurring some 2 weeks previously.

Since 1939 the patient had attended the hospital Diabetic Department; her mild diabetes was well controlled by a low carbohydrate diet. For a number of years the patient had suffered from anginal attacks, and 4 years ago had had a cataract extraction performed on the left eye. She now had a cataract in the other eye. There was no suggestion of any bowel or micturition symptoms.

On abdominal and pelvic examination the only abnormalities discovered were senile vaginitis and a small amount of dirty brown discharge. The uterus was large for a patient of this age.

Examination under an anaesthetic revealed that the discharge was actually faecal material, there being no fistulous opening into the vagina. The cervix was healthy, there was a firm mass approximately 6 inches in diameter attached to the fundus of the uterus. The uterine cavity was 2½ inches long. Scanty, normal-looking curettings were obtained from the uterus. The mass was easily palpable *per rectum* but no added information was obtained.

## INVESTIGATIONS

A barium enema showed signs of diverticulitis in the sigmoid region with a fistula occurring there. The communication seemed to be via a Fallopian tube, body of the uterus and the vagina.

Salpingography revealed a cavity communicating with the lower pole of the uterus and the sigmoid colon. An intravenous pyelogram was normal.

Section of the endometrial curettings showed fragments of non-secretory endometrium together with occasional minute groups of degenerate epithelial cells and fragments of faecal matter.

FIG. 1

Barium enema showing the fistula between the colon and uterus, with barium running down the vagina.

FIG. 2

Salpingogram outlining the uterus and demonstrating the fistula tract.

FIG. 3

Salpingogram showing the fistula and abscess cavity, with a cannula in the uterine cavity.

At this stage a diagnosis of carcinoma of the colon was still a distinct possibility. Accordingly it was decided that a preliminary colostomy should be made; any bowel resection could then be performed at a later date. A staged operation was favoured as the patient was a diabetic subject and 74 years of age.

Laparotomy was performed through a right paramedian incision. The pelvic mass was found to consist of large bowel, omentum, and a loop of small bowel attached to the uterus on the right side. There was no certain evidence of malignant disease. A loop of transverse colon was exteriorized to form a colostomy; this was opened 4 days later. After an interval of 2 weeks a further laparotomy was performed with the object of removing the genital organs and the section of the colon involved in the fistula. A loop of sigmoid colon, omentum, uterus and bladder were all matted together forming a chronic inflammatory mass. The sigmoid colon and omentum were dissected free, the bladder was found to be adherent, and whilst this was being separated a chronic abscess cavity was opened. Pus and faecal matter were removed from the cavity which was low down, antero-lateral to the uterus beneath the bladder. The uterus was freed from the pelvis leaving it adherent to the indurated mass incorporating a loop of sigmoid colon. At this point in the operation it had been anticipated that resection of the colon would be needed. However, by careful dissection it was possible to free the colon from the uterus all except one small area low down on the right side. This remaining attachment of the uterus to the colon was merely a fistulous opening; no bowel resection was necessary. The uterus was removed and the small fistulous opening into the colon was easily closed; a long pelvic appendix was then removed. A blood transfusion of two pints was given during the operation.

In the post-operative period the wound became infected and broke down slightly near the colostomy. Three weeks later the colostomy was closed extraperitoneally. The patient was transferred to a convalescent home after a further three weeks, and was perfectly well when seen in the post-operative clinic.

## Discussion

In the case described the fistula was in all probability the end result of a chronic abscess discharging into the uterus. From the site of the abscess, low down at the side of the uterus almost under the bladder, it was surprising that the bladder was not involved rather than the uterus.

The sigmoid colon tends to migrate posterior to the bladder, and in the female must come in contact with the uterus. This posterior disposition of the colon, plus the presence of the uterus and Fallopian tubes affords a measure of protection to the female bladder, and accounts for vesico-colic fistulae being 5 times more common in the male (Laufman, 1941). Fistula formation follows upon inflammation, and before a fistula can develop some local adhesions must be formed.

Maxwell-Telling and Gruner (1916) found that adhesions between diverticula and the uterus were present in only 5 cases out of a total 280 cases where adhesions were noted. This fact must have some bearing on the rarity of utero-colic fistulae. The uterus, besides providing a mechanical obstacle to fistula formation between the colon and bladder, seems to remain free of adhesions, possibly due to the fibrous consistency and the relatively poor response to inflammatory reaction occurring outside it.

Malignant disease must always be excluded when vaginal discharge occurs in a post-menopausal patient. In the case described the initial diagnosis was that of possible carcinoma of the corpus. This diagnosis was particularly favoured as the patient was a diabetic; Way (1954) maintains that there is an increased incidence of carcinoma of the corpus in the diabetic subject.

## Investigations

Examination under anaesthetic excluded a cervical or uterine carcinoma, but revealed the presence of faecal material and a fistula. Johnson and Stubbs (1950) found that X-ray examination using barium did not demonstrate the fistula. In this case the fistula was detected using barium, but the abscess cavity and the true nature of the fistula were seen much more clearly when salpingography was performed.

## Treatment

Well tried surgical methods were adopted in the management of the case, particularly as the patient was 74 years old and a diabetic. A preliminary colostomy often allows a small fistula to close off, making the resection easier and safer. However, primary resection is now a satisfactory operation since the advent of chemotherapy, and in all probability this would have been a safer and simpler operation.

## Summary

A case of diverticulitis with utero-colic fistula formation is presented. Some of the reasons for the apparent rarity of the condition are discussed.

I am indebted to Mr. J. H. Peel for permission to publish this case, and to Mr. H. A. Burgess for kindly reproducing the X-ray films.

## References

Arnheim, E. E. (1940): *Ann. Surg.*, **112**, 352.

Bacon, H. E. (1949): *Anus, rectum, sigmoid colon: diagnosis and treatment*. 3rd ed. Lippincott, Philadelphia.

Cox, L. W. (1952): *J. Obstet. Gynaec. Brit. Emp.*, **59**, 523.

Johnston, M. H., and Stubbs, G. M. (1955): *Ann. Surg.*, **141**, 138.

Laufman, H. (1941): *Int. Abstr. Surg.*, **73**, 222.

Maxwell-Telling, W. H., and Gruner, O. C. (1916): *Brit. J. Surg.*, **4**, 468.

Ransom, H. K. (1954): *Gastroenterology*, **25**, 12.

Way, S. (1954): *J. Obstet. Gynaec. Brit. Emp.*, **61**, 46.

# MEGALOBLASTIC ANAEMIA OF PREGNANCY AND THE PUERPERIUM

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THE disease which is now called megaloblastic anaemia of pregnancy and the puerperium, was first recognized by Walter Channing of Boston, Massachusetts in 1842. Osler in 1919 reported 2 cases of an Addisonian type of anaemia associated with pregnancy and the puerperium, and further descriptions of the disease were published by Evans (1929) and Whitby (1932). The megaloblastic type of bone marrow was first described by Heilbrun in 1936, and since then several series of cases have been reported (Davidson, Davies and Innes, 1942; Callender, 1944; Thompson and Ungley, 1951; Clark, 1952; Badenoch, Callender, Evans, Turnbull and Witts, 1955; Lowenstein, Pick and Philpott, 1955).

A review of the literature suggests that anaemia of this type is uncommon, for most series of cases have been collected in university departments of haematology, where probably there has been some special selection, and in addition most of the series of cases have been collected over a considerable period of time. For instance, Thompson and Ungley (1951) reviewed 45 cases which had been seen during a period of 17 years, and at the Haematological Department of the Royal Infirmary of Edinburgh 43 cases were seen during a period of 12 years (Clark, 1952). Fifteen of the Edinburgh cases were referred from the Simpson Memorial Maternity Pavilion over a period of 7½ years, during which time there was a total of 31,755 obstetric admissions. The incidence of the disease was higher at the Royal Victoria Montreal Maternity Hospital, where 18 cases were seen during a period of 3 years (Lowenstein, Pick and Philpott, 1955), and at the Rotunda Hospital, Dublin 14 cases were seen in 1 year, an incidence of 1 case in every 288 pregnant women (Lillie, Gatenby and Moore, 1954).

Our experience at Whiston Hospital shows that this type of anaemia must be relatively common, and we have studied a series of 21 cases, of which 19 were seen during the 2-year period between December, 1953 and December, 1955. Five of these 19 patients were admitted to hospital after being delivered at home, and the other 14 patients were delivered in the Hospital Maternity Department. There were approximately 2,700 confinements at Whiston Hospital during the same period, and so the case incidence was about 1 in every 190 hospital confinements. The actual case incidence is probably higher than this, because a study of the Maternity Department records revealed several cases of anaemia which were probably megaloblastic but which have not been included because the investigations were inconclusive.

## Clinical Features

The age of the patients varied between 21 and 41 years. Only 7 of the patients were below the age of 30 and the mean age was 31 years.

All the patients were multiparous, and 12 patients had had more than 3 previous pregnancies. The mean number of previous pregnancies was 4. Two patients were seen with megaloblastic anaemia in 2 successive pregnancies during a period of 2 years. Previous pregnancies were complicated by 1 miscarriage in 5 patients, toxaemia in 2 patients, ante-partum haemorrhage in 1 patient, and post-partum haemorrhage in 2 patients. There was a record of anaemia in the preceding pregnancy in 2 patients, the haemoglobin values being 57 per cent and 61 per cent respectively, but the type of anaemia was not determined.

The anaemia was detected during pregnancy in 10 patients and in the puerperium in 8 patients. Three patients were first seen during labour. The earliest stage when the diagnosis was made was in the 28th week of pregnancy and the latest stage was 6 months after confinement. Fourteen patients were first seen within 2 weeks either before or after delivery. The time of onset of the anaemia is often difficult to determine for the disease is usually well established when the patient is first seen. It seems probable, however, that the anaemia usually develops within the last 3 months of pregnancy. For example, one of our patients was first seen in the 28th week of pregnancy when she gave a history of symptoms of anaemia for 1 month. At that time she had a mild normochromic anaemia (red blood cells 3,200,000 per cubic millimetre; haemoglobin 65 per cent; mean corpuscular volume 97 cubic microns; mean corpuscular haemoglobin concentration 31 per cent) and the sternal marrow was normoblastic. We next saw her 2 weeks after confinement when she had a severe megaloblastic anaemia. Another patient had a mild normochromic anaemia (red blood cells 3,550,000 per cubic millimetre; haemoglobin 72 per cent) at the 30th week of pregnancy, but 7 weeks later the haemoglobin value had dropped to 23 per cent.

Post-partum haemorrhage occurred in 3 patients who were first seen in the puerperium, and in 2 patients seen during pregnancy. One patient in whom anaemia was first diagnosed in the puerperium, had a severe ante-partum haemorrhage due to placenta praevia and required a Caesarean section. One patient had vulval oedema and required Caesarean section, and 2 had slight albuminuria. Three patients were delivered of stillborn babies and one patient had twins. Other associated diseases were an abscess of the thigh, broncho-pneumonia, a urinary infection and infected retained products of conception.

All the patients complained of symptoms of anaemia, namely lassitude and weakness. Anorexia was a frequent symptom. Usually the onset of the anorexia occurred at the same time as the symptoms of anaemia and the appetite improved when the anaemia had been corrected. Eight patients had excessive and prolonged vomiting during pregnancy, and 4 patients complained of a sore tongue.

We have gained the impression that the incidence of uncooperative and difficult patients, particularly those in the puerperium, is greater than usual. Several patients required constant persuasion to stay in hospital, and 4 patients in the puerperium left hospital against advice when they were still very anaemic. One reason for these patients' anxiety to return home is that they have large young families to be cared for.

The anaemia was associated with glossitis (4 patients), splenic enlargement (5 patients), and oedema of the ankles or sacrum (12 patients). Pyrexia occurred in 12 cases, in 4 of which it was associated with an abscess of the thigh, infected retained products of conception, a urinary infection and broncho-pneumonia respectively. In the remaining 8 patients who had no evidence of sepsis, the pyrexia settled when the anaemia was corrected. Examination of the nervous system revealed no abnormality.

Loss of weight was a frequent symptom, and on examination many of the patients appeared to be underweight, although this was not invariable. We consider that loss of weight was more probably a result of the disease than an aetiological factor. Ten patients, of whom one was 30-weeks pregnant and 9 were in the puerperium, were weighed at the time when they were first seen. The weights varied from 6 stones 10 pounds to 10 stones 11 pounds, and in 7

patients the weights were between 7 stones 12 pounds and 9 stones 8 pounds. The mean weight was 8 stones 11 pounds. The patients usually gained weight after the anaemia had been corrected. The weights of 7 patients were recorded a few months after the onset of treatment. One patient lost 3 pounds and the other 6 patients gained 3 stones, 2 stones 6 pounds, 11 pounds, 9 pounds, 6 pounds and 6 pounds respectively. One of these patients who developed anaemia during 2 successive pregnancies, weighed 8 stones 3 pounds on the first occasion. After treatment her weight rose to 11 stones 3 pounds, but it fell to 9 stones 6 pounds during the next puerperium.

Most of the patients had been receiving a poor diet, but not infrequently this was due to the anorexia which developed with the anaemia. Prior to the onset of anorexia the diet sometimes appeared to be adequate. A dietary survey was carried out by the dietician in 6 cases. In 4 of these cases, the diet had been totally inadequate, with the exception of carbohydrate, both before and during pregnancy. In the other 2 cases, the diet had been quite good up to the latter months of pregnancy, when it deteriorated.

## Laboratory Investigations

### *Peripheral Blood*

The number of red blood cells varied between 0·6 and 2·8 millions per cubic millimetre (average 1·45 million per cubic millimetre) and was below 1·8 million in 16 cases. The haemoglobin values (100 per cent=14·8 g. per 100 ml.) ranged from 13 to 70 per cent with a mean figure of 37 per cent (5·4 g.). In most cases there was considerable anisocytosis with a predominance of macrocytes. The mean corpuscular volume varied between 88 and 124 cubic microns with a mean figure of 105·5 cubic microns. The red cells were usually normochromic and the mean corpuscular haemoglobin concentration was below 30 per cent in only 1 case.

Examination of stained blood films showed megaloblasts in 5 cases and normoblasts in 5 cases. Both megaloblasts and normoblasts were seen in the blood films in 2 of these cases. The number of reticulocytes was increased in 7 cases, 5 of which were in the puerperium. The largest number of reticulocytes, 10 per cent and 38 per cent respectively, occurred in 2 patients in the puerperium. This was considered to be evidence that the anaemia was recovering spontaneously, and in 1 of these patients the blood picture returned to normal without treatment with folic acid or vitamin $B_{12}$.

The white blood cells numbered between 3,500 and 11,000 per cubic millimetre in 16 cases, and there was a leucocytosis in the other 5 cases. There was no associated sepsis in the patients with a leucocytosis. Immature white cells varying in number from 1 to 17 per cent were seen in 7 cases, which include the 5 cases with a leucocytosis, but otherwise the differential white cell counts were within normal limits. In 5 cases the presence of immature white cells was associated with an increase in the number of reticulocytes.

The serum bilirubin was estimated in 5 patients, in 2 of whom the figure was raised to 1 mg. and 1·4 mg. per cent respectively and there was a faintly positive indirect van den Bergh reaction. The figure was below 1 mg. per cent in the other 3 patients.

### *Bone Marrow*

Sternal puncture was performed in 18 patients, and in 1 patient who had a megaloblastic anaemia in 2 consecutive pregnancies the marrow was examined during both pregnancies. Megaloblasts were invariably present in the marrow, which was often indistinguishable from that in Addisonian pernicious anaemia. In 6 cases there was a dimorphic marrow picture, with simultaneous normoblastic and megaloblastic erythropoiesis. Macromyelocytes were frequently seen in the marrow.

The marrow changes probably do not usually develop before the last 3 months of pregnancy. In 1 patient examination of the marrow at the 28th week of pregnancy, when the haemoglobin value was 65 per cent showed no abnormality, but 2 weeks after confinement the marrow was megaloblastic.

### *Gastric Acidity*

This was measured in 10 patients by fractional test meal, and in 12 patients by the "Diagnex" method (Conway and Meikle, 1953). The gastric acidity was measured by both methods in 5

patients, and the same results were obtained. Histamine was given to those patients who had no free acid in the resting juice, and to all the patients who had the "Diagnex" test. Achlorhydria was found in 4 of the 17 patients.

## Diagnosis

The diagnosis of a megaloblastic type of anaemia was confirmed in 18 patients by examination of the bone marrow and in 1 patient by the presence of megaloblasts in the peripheral blood. The other 2 patients had a severe macrocytic anaemia, which was corrected by folic acid and vitamin $B_{12}$ respectively and there has been no relapse 7 months and 13 months after stopping treatment.

The presence of a megaloblastic marrow does not establish the diagnosis completely and Addisonian pernicious anaemia and steatorrhoea have to be considered. Addisonian pernicious anaemia was excluded in 13 patients by the presence of free hydrochloric acid in the gastric juice, and in 7 patients by the absence of a relapse during a period of between 6 months and 2 years after stopping treatment. In the other patient pernicious anaemia has not been completely excluded, although the age incidence and the onset of symptoms during pregnancy make this diagnosis unlikely. Steatorrhoea has not been excluded in our patients by fat balance tests, but there was no clinical evidence to support this diagnosis.

Before confirming the presence of a megaloblastic marrow the anaemia may be attributed to iron deficiency, ante-partum or post-partum haemorrhage, pre-eclamptic toxaemia or puerperal sepsis. One patient who had a severe antepartum haemorrhage due to placenta praevia followed in the puerperium by loss of hair and a considerable fall in weight, was considered originally to have developed hypopituitarism.

## Treatment and Prognosis

Fourteen patients were treated with either oral or intramuscular folic acid, 5 patients were treated with intramuscular vitamin $B_{12}$, 2 patients received intramuscular liver therapy, and 1 patient received 2 pints of blood and recovered without further treatment.

### *Folic Acid*

There was a good response in all the patients treated with folic acid. Two patients received 100 mg. folic acid daily, and in the other patients the dose varied between 15 and 30 mg. daily. Three patients were given the folic acid parenterally on account of vomiting, and all the other patients received the folic acid by mouth. The treatment was continued until the anaemia was corrected, except in 4 patients who left hospital against advice. In 9 patients the good response to treatment was judged by an increase in reticulocytes followed by a rise in the haemoglobin and the number of red cells. The reticulocyte response was not measured in 3 patients, in whom there was a satisfactory rise in haemoglobin, and there was a good reticulocyte response in 2 patients, who left hospital before the haemoglobin had risen.

Treatment was started during the puerperium in 6 patients and before delivery in 7 patients. In 1 patient who was seen during 2 successive pregnancies, treatment was started during pregnancy on the first occasion and during the puerperium on the second occasion. Treatment was started within the last 9 days of pregnancy in 5 patients, and in the 28th, 31st and 34th week of pregnancy respectively in 3 patients.

### *Vitamin $B_{12}$*

This produced a good response in all 5 patients, one of whom received vitamin $B_{12}$ therapy during 2 successive pregnancies. The total dose varied between 1,000 and 3,000 microgrammes, and was given in divided doses of 100 microgrammes daily for 1 to 3 weeks and then at weekly intervals. Treatment was started during the puerperium in all the patients, and in 1 patient the blood picture showed evidence of active erythropoiesis before the onset of therapy. The diagnosis of Addisonian pernicious anaemia has not been completely excluded in 1 patient, who has achlorhydria and who has not yet been followed up after stopping treatment.

### *Liver*

The anaemia was corrected in 1 patient by parenteral crude liver extract. One patient failed to respond to intramuscular adminis-

tration of refined liver extract, but subsequently responded to folic acid therapy.

*Blood Transfusion*

The only indications for blood transfusion are emergency Caesarean section and ante-partum or post-partum haemorrhage, which lead to a dangerous situation when they occur before the megaloblastic anaemia has been corrected. Nine patients received transfusions of 1 or 2 pints of blood, and 1 patient received 4 pints at the time of delivery, which occurred 6 months before the correct diagnosis was made. The indication for transfusion was post-partum haemorrhage in 4 patients, ante-partum haemorrhage in 1 patient, and Caesarean section for vulval oedema in 1 patient. There was no absolute indication for blood transfusion in the other 4 patients.

*Iron*

After the anaemia has been partially corrected by folic acid or vitamin $B_{12}$ there is often a fall in the mean corpuscular haemoglobin concentration, which indicates that iron is required in order to restore completely the haemoglobin value and the number of red blood cells to normal. The majority of our patients received iron therapy, although often for only a short period of time. However, the anaemia was corrected in 7 patients, who never received iron therapy.

*Progress*

A follow-up examination of this series of cases was carried out. Two cases had been treated too recently to include in the follow-up examination, and it was impossible to get in touch with 3 patients.

Seven patients were followed-up for over 1 year and 9 patients for between 4 and 9 months after stopping treatment. Four of these patients did not attend the out-patient clinic but wrote to say that they were feeling very well. Nine patients, who attended, were feeling well and their haemoglobin values were over 80 per cent. Two of these patients had originally left hospital when their haemoglobin values were 31 per cent and 37 per cent respectively, and they had not received any further treatment since then.

Three patients had had further pregnancies, during which the anaemia relapsed. Two of these patients were re-admitted under our care, and examination of the bone marrow confirmed that the anaemia was megaloblastic. The other patient, who was confined in another hospital had a haemoglobin value of 47 per cent, but no further investigations were done, and her only treatment was transfusion of 2 pints of blood. When we saw this patient 5 months after confinement, the haemoglobin value had risen to 77 per cent.

## Discussion

Megaloblastic anaemia of pregnancy and the puerperium is a relatively common disease and the diagnosis must often be missed because of inadequate investigation. The diagnosis can be established occasionally from the appearance of the blood, but the only reliable method of confirming the diagnosis is by examination of the bone marrow. It is advisable, therefore, unless the anaemia is markedly hypochromic and responding to iron therapy, to examine the bone marrow of all women in the last trimester of pregnancy or the puerperium who have a red cell count below 3 million per cubic millimetre and a haemoglobin value below 60 per cent.

Establishing the correct diagnosis is of more than academic interest. Firstly, it should avoid blood transfusions which are often given unnecessarily to anaemic women during pregnancy and the puerperium. Secondly, when the diagnosis is made before the last 2 to 3 weeks of pregnancy, the haemoglobin can be raised to a reasonable level before delivery. Thirdly, although the anaemia often improves spontaneously during the puerperium, recovery is slow and often incomplete and many months of ill-health can be avoided by correct treatment.

In temperate climates treatment with both folic acid and folinic acid produces a good response (Spies, 1946; Thompson and Ungley, 1951; Davidson and Girdwood, 1951; Clark, 1952; Israëls and Da Cunha, 1952; Lowenstein *et al.*, 1955). During the puerperium the response is invariably good, but occasionally during pregnancy folic acid fails to produce any improvement (Badenoch *et al.*, 1955). The response to vitamin $B_{12}$ is variable and appears to depend on the size of the dose. There was no

response in 5 cases treated by Clark (1952) with single injections of between 10 and 120 microgrammes, and in 5 cases treated by Thompson and Ungley (1951) with single injections of 80 microgrammes. On the other hand, Moore, Lillie and Gatenby (1955) obtained a satisfactory response in 13 out of 17 patients by giving doses of between 460 and 5,000 microgrammes, and Badenoch *et al.* (1955) obtained a response in 1 out of 3 patients who were given 2,000 microgrammes. Lowenstein *et al.* (1955) obtained a response in 1 patient with oral vitamin $B_{12}$, and in 3 out of 7 patients with parenteral vitamin $B_{12}$, but the dose is not stated. We have given vitamin $B_{12}$ in divided doses up to a total of 1,000 to 3,000 microgrammes to 5 patients, 1 of whom was treated after 2 pregnancies, and have obtained invariably good results. In the tropics, the response to both folic acid and vitamin $B_{12}$ is variable, and often both these substances are required in order to correct completely the anaemia (Das Gupta, Chatterjea and Basu, 1953).

The prognosis for the mother is good and relapse does not usually occur after stopping treatment. On the other hand, the condition is liable to recur during further pregnancies. Evans (1929), Callender (1944) and Clark (1952) all found that recurrence was frequent during subsequent pregnancies. On the other hand, Thompson and Ungley (1951) found that only 1 out of 15 patients developed megaloblastic anaemia during a subsequent pregnancy. In our series the anaemia recurred in 3 patients, who were followed up during 2 successive pregnancies, and in another 2 patients there is a record of a moderate degree of anaemia in the preceding pregnancy. The incidence of recurrence seems sufficiently high, therefore, to justify the prophylactic administration of folic acid during the latter months of subsequent pregnancies. But we do not think that the incidence of the disease is sufficiently high to warrant the routine administration of folic acid to all pregnant women, as suggested by Lowenstein *et al.* (1955).

The aetiology of the disease remains obscure. The evidence favours a deficiency of folic acid rather than vitamin $B_{12}$ for the response to folic acid is usually good whereas the response to vitamin $B_{12}$ is uncertain and only occurs when the dose is large. In addition, the absorption of vitamin $B_{12}$ is normal (Badenoch *et al.*, 1955), and the serum level of vitamin $B_{12}$ is usually within normal limits (Mollin and Ross, 1954; Badenoch *et al.*, 1955; Girdwood, 1956). The effective action of large doses of vitamin $B_{12}$ may be produced by mobilizing the available folic acid and converting it into a more active form. Mueller and Will (1955) suggest that vitamin $B_{12}$ participates in the breakdown of folic acid conjugates in the food into folic acid, and Spray and Witts (1952) postulate that vitamin $B_{12}$ may be responsible for the conversion of folic acid into folinic acid (Citrovorum factor).

The possible causes of the folic acid deficiency are dietary deficiency, a defect in folic acid metabolism, or poor absorption associated with occult steatorrhoea. Davidson (1948), Tuck and Whittaker (1950) and Thompson and Ungley (1951) have each described a case of megaloblastic anaemia in pregnancy in which there was slight impairment of fat absorption. On the other hand, fat absorption was within normal limits in 6 cases investigated by Badenoch *et al.* (1955), and there was no evidence of malabsorption of folic acid in 14 cases investigated by Girdwood (1956). Fat balance tests were not done on our cases, but there was no clinical evidence of steatorrhoea. There seems no doubt, therefore, that, although megaloblastic anaemia in pregnancy may be due occasionally to steatorrhoea, this is not the usual cause of the disease.

Some patients had been taking an inadequate diet, but in other cases the diet appeared to be reasonably good until the latter months of pregnancy when anorexia develops with the anaemia. A full diet survey was carried out on 6 patients and this showed that 2 patients had been taking a satisfactory diet before the development of symptoms of anaemia, whereas the other 4 had been taking a very poor diet. The fact that most of the patients have large families suggests that the diet may often be inadequate, for it has been shown that the amount of meat and fresh vegetables eaten by each member of families with four children is only half that eaten by each partner in childless couples (Ministry of Agriculture, Food and Fisheries, 1955).

Although dietary deficiency is probably a

contributory factor in many cases, the following points suggest that it is not the only cause:

(1) In some cases the diet appears to be adequate.
(2) The members of the vitamin B complex, which include folic acid, are so closely associated in nature that it must be rare for only one to be deficient.
(3) Iron deficiency, which would be expected in multiparous women on a deficient diet, is by no means invariable.
(4) Folic acid must be available in those patients who respond to vitamin $B_{12}$.
(5) Some patients do not respond to combined treatment with folic acid and vitamin $B_{12}$ during pregnancy, but respond during the puerperium (Badenoch *et al.*, 1955).
(6) Dietary deficiency is unlikely in those women who make a spontaneous recovery immediately after pregnancy.

It has been suggested that a defect in folic acid metabolism may be an important aetiological factor. Mueller and Will (1955) postulate that this defect probably occurs in the formation of folinic acid co-enzyme, which converts folinic acid into active folic acid like substances. If this were the case, however, folic acid therapy should not be effective, unless the large doses which are given overcome this defect by mass action. The good response to folic acid and folinic acid therapy suggests that the metabolic defect may occur during the stage of conversion of folic acid conjugates in the food into folic acid.

Since concluding the study of this present series of cases, we have treated 5 further cases with 30 mg. of folic acid conjugate (pteroyltriglutamic acid) given orally in 3 daily doses of 10 mg. All these cases showed a good response, as judged by the height of the reticulocyte response, the rise in haemoglobin level, and the increase in the number of red blood cells, which suggests that the production of folic acid from folic acid conjugate is not defective. However, in view of the fact that the amount of folic acid conjugate given to these patients was much greater than that in the food, no definite conclusion can be made from these results.

In conclusion, it seems probable that in temperate climates defective utilization of folic acid is the most important factor in the production of megaloblastic anaemia of pregnancy, but that the anaemia is particularly liable to occur when defective utilization is associated with a poor diet. This view, however, requires confirmation and there is a need for much further work on the subject.

## Summary

Megaloblastic anaemia of pregnancy and the puerperium is a relatively common disease, and we have seen 19 cases at Whiston Hospital over a period of 2 years. The diagnosis may often be missed because of inadequate investigation, and it is advisable to examine the bone marrow of pregnant or puerperal women with moderate or severe anaemia unless the anaemia is markedly hypochromic and responding to iron therapy.

Treatment with folic acid produces a good response. Vitamin $B_{12}$ also produces a good response when a large dose is given. The occurrence of even a small ante- or post-partum haemorrhage before the anaemia has been corrected may make the patient's condition very serious, and is the only real indication for blood transfusion.

The prognosis after stopping treatment is good except during a subsequent pregnancy when a recurrence of the megaloblastic anaemia is common. During subsequent pregnancies, therefore, the patient should be kept under careful observation and the prophylactic administration of folic acid seems justified.

The aetiology is discussed, and it is concluded that a defect in folic acid metabolism is frequently the basic cause, but that inadequate diet is an important contributory factor.

## Acknowledgments

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## References

Badenoch, J., Callender, S. T., Evans, J. R., Turnbull, A. L., and Witts, L. J. (1955): *Brit. med. J.*, **1**, 1245.
Callender, S. T. E. (1944): *Quart. J. Med.*, n.s. **13**, 75.
Channing, W. (1842): *New Engl. Quart. J. Med. Surg.*, **1**, 157.
Clark, J. R. (1952): *Edinb. med. J.*, **59**, 274.

Conway, H., and Meikle, R. W. (1953): *Brit. med. J.*, **2,** 1019.
Das Gupta, C. R., Chatterjea, J. B., and Basu, P. (1953): *Ind. med. Gaz.*, **88,** 102.
Davidson, L. S. P. (1948): *Blood*, **3,** 107.
Davidson, L. S. P., Davies, L. J., and Innes, J. (1942): *Brit. med. J.*, **2,** 31.
Davidson, L. S. P., and Girdwood, R. H. (1951): *Lancet*, **2,** 1193.
Evans, W. (1929): *Lancet*, **1,** 14.
Girdwood, R. H. (1956): *Quart. J. Med.*, n.s. **25,** 87.
Heilbrun, N. (1936): *J. Amer. med. Ass.*, **107,** 27.
Israëls, M. C. G., and Da Cunha, F. A. L. (1952): *Lancet*, **2,** 214.
Lillie, E. W., Gatenby, P. B. B., and Moore, H. C. (1954): *Irish J. med. Sci.*, 6th ser., 304.
Lowenstein, L., Pick, C., and Philpott, N. (1955): *Amer. J. Obstet. Gynec.*, **70,** 1309.
Ministry of Agriculture, Fisheries and Food (1955): *Domestic food consumption and expenditure, 1953. Annual report of the National Food Survey Committee.* H.M. Stationery Office, London.
Mollin, D. L., and Ross, G. I. M. (1954): *Proc. R. Soc. Med.*, **47,** 428.
Moore, H. C., Lillie, E. W., and Gatenby, P. B. B. (1955): *Irish J. med. Sci.*, 6th ser., 106.
Mueller, J. F., and Will, J. J. (1955): *Amer. J. clin. Nutr.*, **3,** 30.
Osler, W. (1919): *Brit. med. J.*, **1,** 1.
Spies, T. D. (1946): *J. Amer. med. Ass.*, **130,** 474.
Spray, G. H., and Witts, L. J. (1952): *Brit. med. J.*, **2,** 62.
Thompson, R. B., and Ungley, C. C. (1951): *Quart. J. Med.*, n.s. **20,** 187.
Tuck, I. M., and Whittaker, N. (1950): *Lancet*, **1,** 757.
Whitby, L. E. H. (1932): *J. Obstet. Gynaec. Brit. Emp.*, **39,** 267.

# CARCINOMA OF THE VULVA—A REVIEW OF 71 CASES

BY

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THIS paper is based on a series of cases all under the care of, and operated upon by Mr. D. W. Currie, of Leeds, to whom I am indebted for permission to use this material.

Malignant disease of the vulva is a relatively uncommon condition in gynaecological practice to the extent that even a particularly interested surgeon will not see more than 2 or 3 cases in a year. For this reason, up to 1940 when Taussig's principal paper appeared, the condition was treated with sporadic interest and incomplete understanding, and by varied approaches and techniques. Results of the order of 30 per cent or less, of 5-year cures, were regarded with complacency. Another reason for this attitude was the feeling that, because the disease was one of elderly women, too much should not be expected by way of lengthy cures. This was expressed by Taussig himself when he said that the expectancy of life in the sixties, when most of the cases occur, was 10 years or less. Against this, it is interesting to note that the Registrar-General's figures for the expectation of life of women in this country today is still at least 5 years at the age of 80.

The management of cases of vulval malignant disease during the last 15 years has excited more interest and has been more closely studied than hitherto. Under the lead of Taussig, using a technique suggested by Bassett as long ago as 1912, many surgeons have adopted more and more extensive operations, culminating in that preferred by Way. In spite of claims of surprisingly good results using these methods, two other effects have manifested themselves. Firstly, the numbers operated upon are necessarily fewer (Taussig, 70 per cent; Way, 87 per cent) and, secondly—a much more important outcome—the operative mortality has risen to an average figure of 16 per cent in the most skilled hands. Unless cases are collected together for treatment in regional centres—from many points of view an undesirable and often unworkable procedure—mortality figures such as those quoted for these operations must rise further in the hands of surgeons who, managing but 2 or 3 cases a year, will be necessarily less experienced and may possibly be less skilled.

In this state of affairs, it has been thought worthwhile to analyze this series of 71 cases, which have presented themselves during the last 18 years. Of this number only 1 has died in less than 3 months following operation—a mortality rate of 1·4 per cent. Furthermore, in the last five years, 100 per cent of cases seen have been subjected to operation.

The majority of the cases occur in the decade 60 to 69 as in other series. The youngest case is 33 and is still alive and well 7 years later, the oldest was 91 and died of a stroke 4 years after operation (Table I).

TABLE I
*Age Incidence*

| Decade | No. of Cases | |
|---|---|---|
| 30–39 | 2 | |
| 40–49 | 5 | |
| 50–59 | 14 | |
| 60–69 | 25 | |
| 70–79 | 18 | 35·2 per cent of total |
| 80–89 | 5 | |
| 90–99 | 2 | |

It is interesting to note that 25 cases, or 35·2 per cent, occurred in women aged 70 or over.

Most other authors state that about one-third

of the cases occur in nulliparous patients, although Palmer, Sadugor and Reinhard (1949) put the proportion very much lower. Information was available in 62 of this series, and 18 (29 per cent) of these had not borne children.

The commonest sympton was pruritus often of very long standing, and more than half the patients had had a swelling for 3 months or more. Results of treatment undoubtedly depend on the duration of the disease when the patient is first seen, but it is probably unreliable to correlate results purely in relation to size of the lesion. However, taking a diameter of 3 cm. above which a growth is regarded as advanced, 69 per cent of our cases come into this category. Half of these patients did not survive more than 1 year.

A preceding leucoplakia of the vulva is very commonly associated with epithelioma. Taussig (1940) gives the figure as 69 per cent, Way (1951) as 82 per cent, and Palmer *et al.* (1949) only admit to 12 per cent. Details on this point were not recorded in a sufficiently large number of the present cases, but it is more than 60 per cent.

Broder's histological classification has fallen into disuse of recent years, most pathologists relying on a division of cases simply into relatively anaplastic, and relatively well differentiated. The former are less common and only 12 cases in this series were reported as anaplastic growths. Of these none survived more than 1 year, and most workers are agreed that no treatment is really effective against this type of growth.

Malignant infiltration of lymphatic glands according to Taussig (1940), McKelvey (1947), Smith and Pollack (1947) and others is present in about half the cases. But Way in a later publication (1954) finds it in only 32 per cent. In 35 cases of this series, where pathological reports are available, the figure is 60 per cent and the strange fact is, as is remarked by Taussig, that, even if the glands are involved, the same proportion of cases survive as when the glands are entirely free from growth (Table II).

In spite of using a less radical operation, the present results are comparable with those of Taussig, and this fact leads to the conclusion that extension of the operation above the inguinal ligament is unnecessary. To support this,

TABLE II
*Thirty-five Cases with Pathological Reports on Glands*

| 13 Cases Treated Five Years or More Ago | | | 22 Cases Treated in the Last Five Years | | |
|---|---|---|---|---|---|
| Glands Involved | Glands Clear | Survived 5 or More Years | Glands Involved | Glands Clear | Still Alive and Well |
| 6 | – | 5 | 15 | – | 9 |
| | 7 | 5 | | 7 | 4 |

Watson and Gusberg (1946) make the point that, "in extensive operations involving removal of intrapelvic glands, study of reported dissections of retroperitoneal nodes does not indicate that external iliac or obturator nodes are frequently involved".

In the figures concerning gland involvement quoted above, the authors, with the exception of Way, do not distinguish specifically between metastases in the inguinal glands, and metastases in the intra-pelvic glands. Way (1954) in a series of 79 cases found that "9 out of 21 patients with node involvement had their iliac nodes involved as well as the inguinal". Collins *et al.* (1951) approach the matter in the right way by noting the site of origin of all the dissection material. Twenty-five of their cases had gland dissections carried out, and in only 4 were the glands involved; but in 3 of these 4, involvement had occurred to levels far above the pelvic brim. These numbers are too small to be conclusive, but would seem to add weight to the contention that the removal of intra-pelvic glands with an alarming operative mortality is not justified when, in most cases, the disease has probably spread farther afield.

The present series of cases fall naturally into two groups; those operated upon 5 years ago or more, and those treated during the last 5 years. There are 36 in the first group and 35 in the second.

All the 36 cases in the former group have been traced except for 2 which are regarded as deaths. Twenty-one were alive and well 5 years or more after the operation, which represents a 58·3 per cent 5-year cure rate. The operability rate for these cases was 90 per cent. During this earlier period many of the older patients and those in

poor general condition had only a vulvectomy —sometimes not a very radical one—without removal of inguinal glands. Some of these had radium implants or deep X-ray to the inguinal regions, but this as a method of treatment has been abandoned of recent years except for a palliative operation, because the results were found to be less good, the constitutional upset was profound, and the convalescence was frequently stormy.

Fourteen cases had local recurrences successfully treated by further surgical excision. One recurred 18 years, and four 12 years after the original operation. Several had 2 recurrences and one had 3. In 2 of the cases a most advanced recurrence had occurred necessitating exenteration-type operations. One survived only 4 months but the other lived for 3 years. Such procedures are seldom justified.

Of the 18 deaths that have been fully traced, 7 were definitely due to causes other than carcinoma, and the remaining 11 all died from extension of the disease. Six of these occurred in less than a year, of which 4 had had palliative vulvectomies for very advanced growths. In spite of the fact that not many of these cases survive more than a few months, it is felt that a palliative vulvectomy has a definite place in the management of carcinoma of the vulva. The patient is relieved of the pain, and both she and her relatives are delivered from the offensiveness and the frequent need for dressings of a large fungating mass.

There are 35 cases that have been seen and operated upon in the last 5 years; none was denied operation. Thirteen have already died, all except 1 from extension of the disease, and 6 lived less than 1 year. With 100 per cent operability rate, and taking into consideration the fact that only 11 of the 35 cases had growths less than 3 cm. in diameter, the relatively low survival rate is explained. Twenty-two of the cases are alive and well and free from growth (62·9 per cent). Twenty-four cases had the inguinal glands removed, 14 simultaneously with the vulvectomy, and 22 have pathological examinations recorded. Fifteen had involved glands and in 7 cases no metastases were found.

The 3 cases in the 71 which were not epitheliomata were seen during the last 5 years. Two were malignant melanomata and 1 was a fibrosarcoma. One of the cases, a melanoma, died in a very short time, but the other 2 survive.

As regards the operation itself, the ideal that is aimed at, is to carry out simultaneously a bilateral inguinal adenectomy through incisions parallel, to and below the inguinal ligament and separated from the vulvectomy by a bridge of skin. If the patient's condition is good, the operation is performed in this sequence, but if she is very old, or her general condition is rather poor, the vulvectomy is done first, and the removal of glands may be deferred for 2 or 3 weeks, or permanently, depending on her condition during the course of the operation. The inguinal glands are removed with the fat of the deep layer of the superficial fascia, largely by finger dissection, over a large area of the femoral triangle. The upper part of the long saphenous vein and the cribriform fascia are removed, and the femoral canal is carefully cleared.

The incisions for the vulvectomy roughly form a diamond shape, and a wide margin of healthy tissue including fat down to the bone is removed with the growth. In the performance of this part of the operation, little heed is paid to the subsequent closure. This is regarded as all-important. It is sometimes possible in obese subjects to draw downwards a flap of skin from the abdominal wall to make good the deficiency.

The inguinal incisions are closed with drainage, but the vulvectomy area where necessary is left to granulate without skin-grafting. Although in elderly patients there is invariably some sloughing of the edges of the inguinal wounds, gross post-operative sepsis is not seen. This is the cause of death in many of Way's cases.

Neither diathermy nor cautery is used. It is felt that healing is better without them, and there is less likelihood of haemorrhage later with all vessels secured with ligatures.

Artificial hibernation anaesthesia is now employed, and blood transfusion is given during operation: the object being, especially in the older patient, only to replace the blood lost. In spite of the recommendations of McKelvey (1947) and others for the supplementary use of local anaesthesia, this has not been considered necessary, especially with the advent of new methods.

The operation with 2 operators working simultaneously on the glands takes about 50 minutes.

The average convalescence is about 6 weeks before the wounds are entirely healed, and during this time careful nursing care has certainly contributed largely, in this series, to the low mortality.

The 1 operative fatality occurred on the third post-operative day from shock and increasing toxaemia. The patient was 73 years old and had a growth that was 13 cm. in diameter. She was subjected to the complete operation, whereas a 2-stage approach would probably have been the wiser course.

## Conclusions

(1) The extent of the vulvectomy must be dictated only by the needs of a complete and widespread excision, without undue insistence on subsequent closure. This policy is frequently alarming but never disastrous and one feels that on it depends this modest success, and by it one hopes that the local recurrence rate will further be reduced.

(2) Keeping in mind the average age and physical condition of the patients, the operation should be carried out with expedition, and although it would appear that a 1-stage operation is desirable, this is by no means insisted upon as a routine procedure.

(3) Extension of the operation above the inguinal ligament is not justified because of the high surgical mortality at the present time, and the risk of this mortality becoming even higher if the operation were to be popularized as a routine procedure; and in spite of the scanty information about the frequency of involvement of intra-pelvic glands, the evidence points to the fact that by the time these glands are involved, the condition has spread far afield, and that this event is a late stage in the disease. How else can one explain the fact first pointed out by Taussig, and fully confirmed by this series, that involvement of the inguinal glands does not adversely affect the prognosis? The tentative hypothesis is offered that apart from anaplastic growths, there is some barrier or hazard at inguinal ligament level which gives pause to the onslaught, but which, when finally surmounted or overcome, leaves the way open for rapid and progressively widespread dissemination.

(4) A palliative vulvectomy should not be withheld from the patient who on some grounds may be considered inoperable. The relief, if only for a short time, to the patient herself and to her attendants is considerable and worth while.

(5) In order to detect the early local recurrence, patients should if possible be followed up at least every 6 months.

(6) The whole complexion of the management of the condition will be altered when patients seek advice earlier than they do at the present time.

## References


Bassett, A. (1912): *Thèse.* Univ. Paris.

Collins, C. G., Collins, J. H., Nelson, E. W., Smith, R. C., and MacCallum, E. A. (1951): *Amer. J. Obstet. Gynec.*, **62**, 1198.

McKelvey, J. L. (1947): *Amer. J. Obstet. Gynec.*, **54**, 626.

Palmer, J. R., Sadugor, M. G., and Reinhard, M. C. (1949): *Surg. Gynec. Obstet.*, **88**, 435.

Smith, F. R., and Pollack, R. S. (1947): *Surg. Gynec. Obstet.*, **84**, 78.

Taussig, F. J. (1940): *Amer. J. Obstet. Gynec.*, **40**, 764.

Watson, B. P., and Gusberg, S. B. (1946): *Amer. J. Obstet. Gynec.*, **52**, 179.

Way, S. (1951): *Malignant disease of the female genital tract.* Churchill, London.

Way, S. (1954): *Brit. med. J.*, **2**, 780.

# EVALUATION OF THE INTRADERMAL COLOSTRUM PREGNANCY TEST

BY

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## INTRODUCTION

AN ideal pregnancy test should be specific for pregnancy from the time of conception, reliable, easy to perform and easy to interpret, inexpensive, giving a rapid result and needing the minimum of equipment. The various biological and hormonal tests all fail to satisfy these criteria. The search for a suitable test has occupied the minds of biologists and obstetricians from time immemorial.

In 1910, Sauerbruch and Heyde, by anastomosing the blood circulation of pregnant and non-pregnant rats, found that labour caused the non-pregnant rat to suffer vomiting, convulsions and finally death. This they explained by postulating a toxin to which the pregnant rat was immune, which increased during labour and affected the non-pregnant rat. This immunity of the pregnant rat indicated a line of research directed towards the discovery of a substance which is present in the pregnant state, without causing reaction, but which could cause reaction in the non-pregnant.

The most convenient site for the study of sensitivity reactions is the skin—and since that time cutaneous tests have been made with many substances (e.g., ox serum, placental extracts, etc.) on pregnant and non-pregnant women in the search for a reliable pregnancy test.

Falls, Freda and Cohen (1941) decided to use colostrum in this way, on the assumption that it was most likely to contain a protein of a different character from other body proteins. They discovered that pregnant women, on intradermal injection of colostrum, gave faint or no response within one hour, while non-pregnant women gave a definite skin reaction. This failure to react is explained by assuming that early in pregnancy the production and absorption of the active substance from the breast leads to an immune state, which prevents local reaction.

The Colostrum Test as performed by Falls, Freda and Cohen (1941) was accurate in 98 per cent of pregnant and 96 per cent of non-pregnant women. Similarly satisfactory results were reported by Martins and Howells (1951) and by Ferrero (1951). Other investigators failed to produce such a high degree of accuracy (Goldman, Kessler and Wilder, 1942; Pulver and Posner, 1942; Allen and Donaldson, 1943).

In view of the obvious advantages of this pregnancy test, it was considered worth while to make yet another attempt at its assessment.

## COLLECTION AND PREPARATION OF THE COLOSTRUM

Colostrum was aspirated from the breasts of primiparae around the 28th week of gestation into sterile 5 ml. rubber-capped bottles, after cleansing the nipple and areola with ether.

Each breast yielded from 2 ml. to 20 ml. of colostrum. The bottles were centrifuged at 4,000 revolutions per minute for 15 minutes. The colostrum was then aspirated into a syringe, leaving the fat particles on the wall of the bottle,

and transferred in 10 ml. amounts into several 25 ml. bottles. A solution of 25 mg. of chloromycetin in 10 ml. of normal saline was added to each bottle containing the colostrum. At the same time control solutions of 25 mg. of chloromycetin in 20 ml. of saline were prepared. Both the colostrum and the control solutions were then placed in a refrigerator where they remained for 10 days prior to their use and where they were stored throughout the time of the investigations.

### Technique of Injection

The flexor surface of the forearm was cleaned; by injecting intradermally amounts varying between 1/50–1/25 ml. of the prepared colostrum, a wheal of approximately 0·5 cm. was raised and the exact diameter recorded. A second wheal of the same size was raised by injection of the control solution.

Reactions were noted and recorded at 15, 30 and 60-minute intervals.

### Method of Investigation

A total of 340 tests was conducted and analyzed:

204 pregnant women.
108 non-pregnant women.
13 men.
10 post-menopausal women.
5 menstruating women.

Four cases showing allergic reaction to the control solution were rejected.

Women giving a history of asthma, allergic rhinitis, urticaria and other allergic phenomena were excluded from the investigation.

### Interpretation

The total reaction to the injection of the colostrum was considered, that is, the size of the wheal, the formation of the red areola and the rate of disappearance of the reaction.

A reaction for pregnancy was considered *positive*, when the following criteria were satisfied:

(1) Absence of wheal enlargement, or only a slight increase in its diameter.
(2) Absence of areola or the presence of only a slight one.
(3) Disappearance of all reaction at the end of 1 hour.

A *negative* reaction for pregnancy consisted of:

(1) Considerable enlargement of the original wheal (over 50 per cent).
(2) Presence of a surrounding red areola of over 1·5 cm. in diameter.
(3) Persistence of the reaction at the end of 1 hour.

Other types of reaction, of which there were many, were considered doubtful.

### Results

Of the 204 pregnant women, 134 showed positive reaction for pregnancy, 22 showed negative reaction and 48 were doubtful.

Of 108 non-pregnant women, 58 showed negative reaction of pregnancy, 14 showed positive reaction and 36 reactions were doubtful.

Of 13 men tested, 4 gave positive reactions for pregnancy, 6 negative and 3 were doubtful.

There were no cases of skin infection.

The results of the tests performed on 10 post-menopausal and 5 menstruating women were not included in Tables I and II. Eight of the 10 post-menopausal women gave positive reactions for pregnancy, the remaining 2 gave doubtful reactions. All the 5 menstruating women showed a positive reaction for pregnancy.

Table I

| | Pregnant | | Non-pregnant | |
|---|---|---|---|---|
| | No. | Per cent | No. | Per cent |
| Wheal increase .. .. | 54 | 26·5 | 70 | 57·8 |
| No wheal increase .. .. | 150 | 73·5 | 51 | 42·1 |
| Areola .. .. .. | 65 | 32·0 | 83 | 68·6 |
| No areola .. .. .. | 139 | 68·0 | 38 | 31·3 |
| Reaction at 60 minutes .. | 71 | 34·9 | 86 | 71·0 |
| No reaction at 60 minutes .. | 133 | 65·1 | 35 | 28·9 |

Some specificity of the reaction to colostrum is demonstrated by Table I: 65–75 per cent of all pregnant women show no sensitivity, while

TABLE II

| | Positive | | Negative | | Doubtful | |
|---|---|---|---|---|---|---|
| | No. | Per cent | No. | Per cent | No. | Per cent |
| 204 pregnant women | | | | | | |
| 4 ectopic .. .. | 4 | 100 | | | | |
| 68 1st trimester .. | 46 | 67·9 | 6 | 8·8 | 16 | 23·5 |
| 65 2nd trimester .. | 43 | 66·1 | 8 | 12·3 | 14 | 21·5 |
| 67 3rd trimester .. | 41 | 61·2 | 8 | 11·9 | 18 | 26·8 |
| 204 women | 134 | 65·3 | 22 | 10·8 | 48 | 23·7 |
| 121 non-pregnant cases | | | | | | |
| 13 men .. .. | 4 | 30·7 | 6 | 46·1 | 3 | 23·0 |
| 108 women .. .. | 14 | 12·9 | 58 | 53·9 | 36 | 33·3 |
| 121 cases .. .. | 18 | 14·8 | 64 | 52·9 | 39 | 32·4 |

60–70 per cent of non-pregnant women show sensitivity.

The test was performed on approximately the same number of pregnant women in each trimester; the accuracy was greatest in the first, while the number of doubtful reactions was highest in the last trimester (Table II).

Four cases of ectopic pregnancy were included in the series, all of which gave a positive pregnancy reaction (Table II). It appears from the literature that other investigators have also found that cases of ectopic gestation give very consistent readings: out of 41 cases, 40 showed positive reaction for pregnancy (Allen and Donaldson 2, 1943; quoted by Falls: Rogers 4 and Cook County Hospital 30, 1943; Colomé 4, 1952).

## CONCLUSION

The temporary immunity to colostrum conferred by pregnancy upon the majority of women is an interesting phenomenon inviting further attention, but as an aid to the diagnosis of pregnancy the intradermal colostrum test is disappointing.

Amenorrhoea at the menopausal age and vaginal bleeding following a period of amenorrhoea are the two conditions in which a differential diagnosis of pregnancy is most frequently needed—and it is just at these times that the test is most unreliable, as during menstruation and at the menopause a positive pregnancy reaction is given.

There is a wide margin of error in both pregnant and non-pregnant cases but the results suggest that this test has some value as an aid to the diagnosis of extra-uterine pregnancy, if taken together with other symptoms and signs.

Interpretation of the reactions is frequently difficult until a number of observations have been made.

## SUMMARY

(1) An Intradermal Colostrum Test for pregnancy is described.

(2) The technique of collection and preparation of the colostrum is given.

(3) Three hundred and forty-four tests were performed and are analyzed.

(4) The test is considered of little value as a general test for pregnancy.

(5) The test may be of some value in cases of extra-uterine pregnancy.

We wish to express our thanks to Miss A. M. Fleming, Mr. J. P. Erskine and Mr. F. Denny for their permission to carry out the investigations and to Dr. J. Fielding for his help with equipment.

## REFERENCES

Allen, E., and Donaldson, L. B. (1943): *Amer. J. Obstet. Gynec.*, **45**, 209.

Colomé, J. G. (1952): *Toko-ginec. pract.*, **104**, 382.

Falls, F. H., and Bartlett, F. K. (1914): *Amer. J. Obstet. Dis. Wom.*, **70**, 910.

Falls, F. H., Freda, V. C., and Cohen, H. H. (1941): *Amer. J. Obstet. Gynec.*, **41**, 431.

Ferrero, N. (1951): *Amer. J. Obstet. Gynec.*, **61**, 672.

Goldman, L. M., Kessler, H. B., and Wilder, M. E. (1942): *J. Amer. med. Ass.*, **119**, 130.

Gruskin, B. (1936): *Amer. J. Surg.*, **31**, 59.

Martins, S. M., and Howells, B. P. (1951): *Ann. west. Med. Surg.*, **5**, 558.

Pulver, M., and Posner, L. B. (1942): *Amer. J. Obstet. Gynec.*, **44**, 690.

Sauerbruch, F., and Heyde, M. (1910): *Münch. med. Wschr.*, **57**, 2617.

Schwartz, E. (1936): *Amer. J. Surg.*, **33**, 225.

# FATAL INTRAPERITONEAL HAEMORRHAGE DURING PREGNANCY

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SPONTANEOUS intraperitoneal haemorrhage in pregnancy is comparatively rare if one is to judge by the few reports in the literature. This rarity and the unusual source of the bleeding would seem to warrant the recording of the strange sequence of events and most tragic outcome in our case.

## CASE HISTORY

Mrs. M.C., a primigravida, aged 37 years, who had been married 5 years, attended the antenatal clinic on 26th November, 1953 in the twelfth week of pregnancy, and was booked for confinement.

The relevant previous medical history was that she had pulmonary tuberculosis in 1948, and this was treated by rest and with a phrenic crush operation. Since her discharge from the sanatorium she had been under the chest physician's surveillance.

Examination showed her to be a healthy woman—no abnormality of the heart or lungs was detected. The blood pressure was 120/70. Examination of the urine for albumen and sugar was negative. On abdominal palpation, the fundus of the uterus was felt just above the symphysis pubis. A pelvic examination was not performed. The patient was blood group O, Rhesus positive. The haemoglobin was 86 per cent (Haldane). The Wassermann reaction was negative. A mass X-ray report commented on a high right diaphragm, but otherwise no abnormality was seen.

### *Progress*

She attended the antenatal clinic regularly, the pregnancy proceeding without incident. When seen on 15th April, 1954 she was in the thirty-second week of pregnancy. The blood pressure was 116/68; the urine did not contain albumen. The height of the fundus was compatible with her dates. The foetal presentation was cephalic, the head being above the pelvic brim, and the foetal heart was heard. The patient was asked to return to the clinic in 2 weeks.

On 26th April a telephone call was received about midday from a general practitioner. He stated that he had been called to see this patient who was complaining of severe lower abdominal pain. There was no external bleeding. He had made a diagnosis of concealed accidental haemorrhage, and requested her admission to hospital.

Preparations were made for the admission but the patient did not arrive. Enquiries were made and it was learned that she had died during the journey to hospital. Her symptoms (of abdominal pain) had increased in severity, the ambulance driver had stopped at the nearest doctor's house, and death occurred whilst she was being examined.

## POST-MORTEM FINDINGS

Autopsy was carried out the following morning.

*External examination.* The body was that of a well-nourished young woman showing pigmentation of the nipples and an enlarged abdomen. There was a small amount of liquor amnii issuing from the vagina.

*Internal examination.* The brain showed no evidence of disease. The lungs showed emphysema. Over the right lower lobe there were some pleural adhesions, and, on cut section, this part of the lung showed old caseous tuberculosis with fibrosis. The heart was about normal in size and showed no gross abnormality.

The peritoneal cavity was distended by a very large quantity of blood and blood clot. On removing the blood, the uterus was found to be unruptured, the ovaries and tubes normal, and the only abnormality seen was a small peritoneal lesion on the lateral pelvic wall at the right side of the pouch of Douglas. This was an

FIG. 1

Low magnification of decidual lesion showing raised edge and haemorrhage. Haematoxylin and Eosin. ×7.

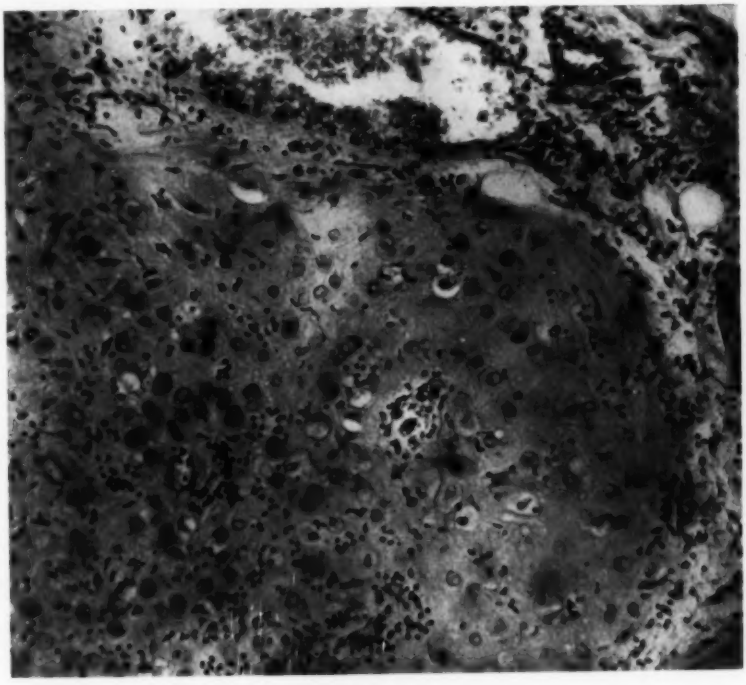

FIG. 2

Higher magnification of area outlined in Fig. 1. Haematoxylin and Eosin. ×140.

oval shaped area 2·5 by 2 cm. with a raised edge and congested papillary floor. There was a little retroperitoneal haemorrhage immediately adjacent to the lesion. As this area appeared to be the site of bleeding it was removed for microscopy.

The liver was pale with a few small ecchymoses beneath the capsule. The spleen was small and congested. The kidneys were extremely pale. The bladder was normal. The gastro-intestinal tract was normal.

The uterus was enlarged to a size corresponding to her dates. It contained a perfectly formed female infant. There was no evidence of placental separation or placental abnormality.

Microscopic examination of the pelvic lesion (Figs. 1 and 2) showed haemorrhagic decidual tissue without chorionic villi. This very vascular decidual reaction was apparently the source of the fatal haemorrhage.

## Discussion

Some of the many possible causes of intra-abdominal haemorrhage in pregnancy are discussed in a review by Roberts (1949), but he does not mention decidual bleeding.

In many of the reported cases, the source of the bleeding had not been discovered. One such case was described by Kenny and Doniach (1945), where a fatal haemorrhage followed coitus in a woman with signs of toxaemia. Other cases without apparent cause have been described by O'Connor and Bradley (1946) and Wengle (1954).

Haultain (1944) reported a massive internal haemorrhage from a lesion on the rectal wall. This was shown to contain decidua and large chorionic villi, and was assumed to be a tubal abortion with re-implantation.

In our case no villi were found and the haemorrhage appeared to originate in highly vascularized decidua. It is known that decidual formation can occur outside the uterus during pregnancy and that such a reaction is most common in an endometriomatous patch. Our sections showed no evidence of endometriosis. An extensive search of the literature produced only one relevant case entitled "Deciduation and massive haemorrhage of the omentum in the final month of pregnancy" (Melody, 1950). Here the bleeding was from the omentum which on section showed an extensive decidual reaction. This would seem to indicate that bleeding can occur from decidual tissue. Furthermore, there are reports of cervical bleeding in pregnancy and post-partum from excessively vascularized decidual tissue beneath the endocervical mucosa.

## Summary

A case of fatal intraperitoneal haemorrhage in a pregnant woman has been recorded. The source of bleeding appeared to be a very vascular decidual reaction on the pelvic peritoneum.

We are indebted to Professor H. C. McLaren for allowing us to refer to the clinical notes on this case.

## References

Haultain, W. F. T. (1944): *J. Obstet. Gynaec. Brit. Emp.*, **51**, 38.

Kenny, M., and Doniach, I. (1945): *J. Obstet. Gynaec. Brit. Emp.*, **52**, 259.

Melody, G. F. (1950): *West. J. Surg. Obstet. Gynec.*, **58**, 460.

O'Connor, C. T., and Bradley, J. J. (1946): *New Engl. J. Med.*, **235**, 648.

Roberts, H. (1949): *J. Obstet. Gynaec. Brit. Emp.*, **56**, 976.

Wengle, E. H. (1954): *Amer. J. Obstet. Gynec.*, **68**, 943.

# GRANULOSA CELL TUMOUR OF THE OVARY

## Report of a Case in a Woman Aged 82 Years

BY

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*Pathologist to The Women's Hospital, Liverpool*

GRANULOSA cell tumours of the ovary occur most commonly between the ages of 40–60 years (Pratt, 1937; Varangot, 1938; Burslem, Langley and Woodcock, 1954), but cases have been known to arise in the young and in the old. It is uncommon for this tumour to be found in persons over 60 years of age. Te Linde (1930) reported 39 cases and his eldest patient was 72 years old. Varangot (1938) in a series of 266 cases recorded 12 cases in the eighth decade, whilst Dockerty and MacCarty (1939) in a series of 30 cases had one person aged 77 years. Henderson (1942) reported 30 cases and his oldest patient was aged 72 years. Hodgson, Dockerty and Mussey (1945) recorded 62 cases and their eldest patient was aged 72 years. Selye (1946) extensively reviewed the literature on granulosa cell tumours of the ovary and he stated that the oldest recorded case was in an individual aged 81 years. Falls, Ragins and Goldenburg (1949) recorded one patient aged 71 years in a series of 20 cases, whilst Jackson and Haines (1950) reported 40 cases their eldest patient being 71 years old. Myhre (1955) has recorded a series of 20 cases and his eldest patient was aged 81 years. Further series of cases have been reported by Lepper, Baker and Vaux (1932), Novak and Brauner (1934), Harvey, Dawson and Innes (1939), Shaw and Gluckman (1939), Ducket, Davies and Fetter (1953), and Nidegger (1954). The authors together had collected 124 cases of granulosa cell tumours of the ovary and the ages of their eldest patients were in the seventh decade of life.

Recently a granulosa cell tumour has been removed successfully from a woman aged 82 years. Since this is the oldest individual in which a granulosa cell tumour has been found, it was considered of interest to report this case.

### CASE REPORT

E.T., aged 82 years, complained of post-menopausal bleeding. The first attack occurred 5 months before the patient was seen and lasted for 14 days. Bleeding recommenced 3 days before she was examined and was accompanied by lower abdominal pain. The patient had had 9 children and 1 stillbirth. The last child had been born when she was 40 years old. Her menopause had occurred at the age of 46 years.

Physical examination confirmed the presence of bleeding from the vagina. The cervix, uterus and appendages were normal, the blood pressure was 210/110 and there was hypertrophy of the left ventricle of the heart. Examination of the other systems revealed no abnormal physical signs.

A diagnostic curettage was performed. Examination of the curettings showed cystic glandular hyperplasia of the endometrium (Fig. 1). It was known that the patient was not receiving oestrogen in any form. Consequently it was deduced that probably she had a granulosa cell tumour. An abdominal laparotomy, therefore, was done when the right ovary was seen to be enlarged. The uterus and both appendages were removed. The patient made an uneventful recovery from the operation.

The right ovary measured 4 cm. by 3 cm. by 2 cm. and its outer surface was smooth. On section the ovarian tissue was found to be replaced by a homogenous yellowish white material. The left ovary and both Fallopian tubes showed no abnormality. The endometrium lining the uterine cavity was bulky.

The normal tissue of the right ovary was replaced by neoplastic material, which on its outer aspect was surrounded by a fibrous capsule. The tumour cells were polyhedral in

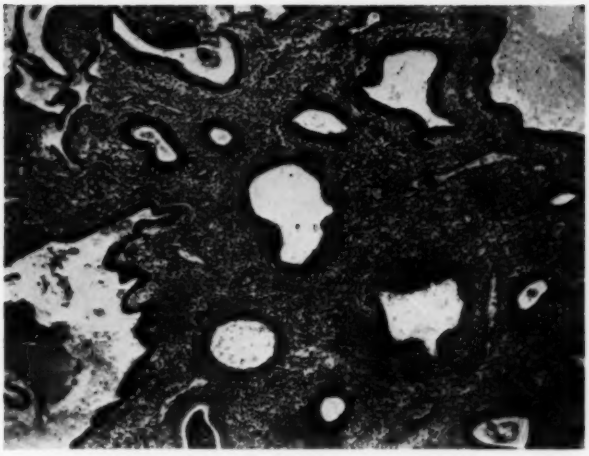

FIG. 1

Curettings showing cystic glandular hyperplasia of the endometrium. × 52.

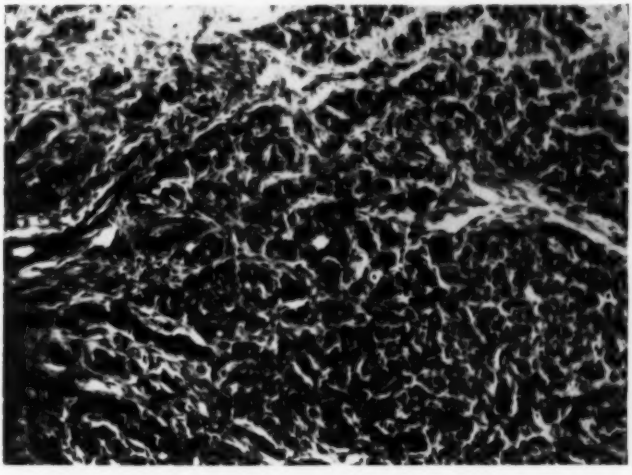

FIG. 2

Granulosa cell tumour of the ovary showing cells arranged in trabeculae and microfollicles. × 104.

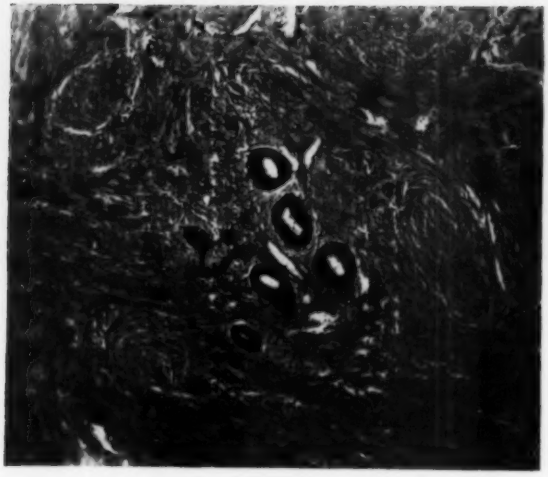

FIG. 3
Section of uterine wall showing adenomyosis interna. ×52.

shape and had round or oval vesicular nuclei, which contained one or two nucleoli. Hyperchromatic nuclei or mitotic figures were seen in a few cells. These cells were arranged either in microfollicles, which resembled Call-Exner bodies, or in trabeculae of varied width and length. The cellular masses were separated from one another by a variable amount of connective tissue (Fig. 2). There was cystic glandular hyperplasia of the endometrium and adenomyosis interna of the myometrium (Fig. 3).

## Summary

A granulosa cell tumour of the ovary is reported occurring in a woman of 82 years of age. This is the oldest case that has been recorded.

The post-menopausal bleeding, the cystic glandular hyperplasia of the endometrium and the adenomyosis interna were caused by the oestrogenic effects of the tumour.

## Acknowledgment

I wish to thank Sir Arthur A. Gemmell for permission to publish this case and for his help in the preparation of this paper.

## References

Burslem, R. W., Langley, F. A., and Woodcock, A. S. (1954): *Cancer*, **7**, 522.

Dockerty, M. B., and MacCarty, W. C. (1939): *Amer. J. Obstet. Gynec.*, **37**, 425.

Ducket, H. C., Davies, C. D., and Fetter, B. F. (1953): *Obstet. Gynec.*, **2**, 611.

Falls, F. H., Ragins, A. B., and Goldenburg, M. (1949): *Amer. J. Obstet. Gynec.*, **57**, 1107.

Harvey, W. F., Dawson, E. K., and Innes, J. R. M. (1939): *Edinb. med. J.*, **46**, 256.

Henderson, D. N. (1942): *Amer. J. Obstet. Gynec.*, **43**, 194.

Hodgson, J. E., Dockerty, M. B., and Mussey, R. D. (1945): *Surg. Gynec. Obstet.*, **81**, 631.

Jackson, I., and Haines, M. (1950): *J. Obstet. Gynaec. Brit. Emp.*, **57**, 737.

Lepper, E. N., Baker, A. H., and Vaux, D. M. (1932): *Proc. R. Soc. Med.*, **25**, 1241.

Myhre, E. (1955): *Acta path. microbiol. scand.*, **36**, 517.

Novak, E., and Brauner, J. N. (1934): *Amer. J. Obstet. Gynec.*, **28**, 637.

Nidegger, J. C. (1954): *Gynaecologia, Basel*, **137**, 129.

Pratt, F. B. (1937): *J. Obstet. Gynaec. Brit. Emp.*, **44**, 880.

Selye, H. (1946): *Encyclopedia of endocrinology. Vol. 7. Ovarian tumors.* Richardson, Bond & Wright, Montreal.

Shaw, W., and Gluckman, J. (1939): *St Bart's Hosp. Rep.*, **72**, 63.

Te Linde, R. W. (1930): *Amer. J. Obstet. Gynec.*, **20**, 552.

Varangot, J. (1938): *J. Chir., Paris*, **51**, 651.

# GRANULOSA CELL TUMOUR OF THE OVARY AT THE AGE OF 85 YEARS

BY

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THE only unusual feature about this case is the late age at which a granulosa cell tumour of the ovary was found and treated.

### *History*

Mrs. J.B., aged 85 years, was admitted as an emergency case to the Liverpool Royal Infirmary on 5th December, 1955, complaining of haematuria of 8-weeks duration, hypogastric pain of 6-weeks duration and vaginal bleeding during the previous 3 weeks. She volunteered the information that her breasts had been swollen for 4 to 5 weeks, 1 year previously. She had married in 1904 but never became pregnant, and separated from her husband in 1913. The menopause had occurred at the age of 45 years.

### *Examination*

The patient was alert and intelligent. The breasts were more youthful in appearance than her years would have suggested.

Abdominal palpation disclosed a firm hemispherical mass arising from the pelvis and extending into the right iliac fossa. There was no evidence of ascites.

Vaginal examination revealed a normal nulliparous cervix with blood exuding from the external os. The vaginal skin was healthy and appeared to be under the influence of oestrogen. The uterus was normal in size for a pre-menopausal woman and was displaced anteriorly and to the left by a firm smooth spherical mass approximately 6 inches in diameter. No nodules were palpable in the pouch of Douglas.

The urine was normal. The deposit showed no evidence of blood cells or other abnormal constituents. The radiographic appearance of both kidneys and ureters was normal. The bladder shadow was indented centrally by a soft tissue mass. The chest X-ray was normal and the electrocardiograph was within normal limits.

### *Blood Examination*

Haemoglobin, 13·8 grammes per cent; White Blood Cells, 5,000 per c.mm.; Serum Urea, 49 mg. per cent.

## OPERATION

It was concluded that the haematuria had in fact been metrostaxis and it was decided to carry out laparotomy. This was performed on 8th December, 1955, through a midline lower abdominal incision. A firm, completely encapsulated, spherical mass 6 inches in diameter replaced the right ovary. The left ovary was small and apparently normal. The uterus was large for the patient's age. Approximately 10 ounces of clear straw-coloured fluid was aspirated from the peritoneal cavity but there was no evidence of malignant peritoneal deposits. There were many firm old peritoneal adhesions throughout the pouch of Douglas suggesting that there had been an inflammatory process many years previously which may have been a factor in her infertility. Total hysterectomy and bilateral salpingo-oöphorectomy was performed. One pint of blood and one half-pint of normal saline were given intravenously on return to the ward. The post-operative period was uneventful except for the patient falling out of bed on the 5th post-operative day, and for a urinary infection due to *Bacterium coli* on the 11th post-operative day. The latter responded satisfactorily to sulphadimidine and alkalis. The patient was discharged home on the 23rd day.

*Follow-up Examination.* On 29th May, 1956, 5½ months after operation, the patient was free from abnormal symptoms except for discomfort and stiffness of both knee joints. The breasts appeared to be slightly smaller than on 5th December, 1955. The abdominal scar was firmly healed throughout. Vaginal examination showed the vault to be well healed and the vaginal skin to be moderately atrophic and not under the influence of oestrogen. There was no palpable evidence of any pelvic abnormality.

*Examination of Specimen.* The specimen consisted of the uterus and cervix together with

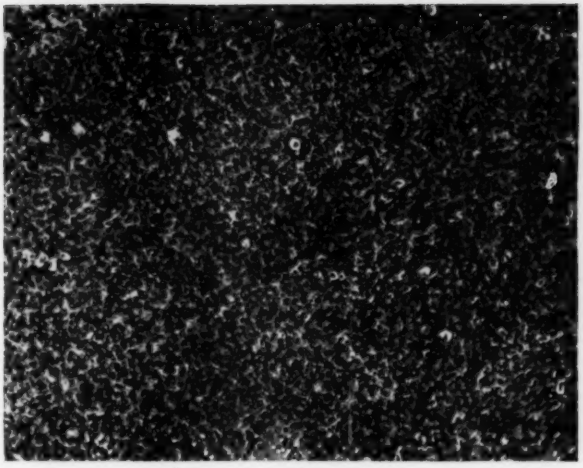

FIG. 1

Granulosa cell tumour of diffuse type showing occasional microcyst formation. H. & E. × 105

FIG. 2

Endometrium showing cystic hyperplasia. H. & E. × 85.

both tubes and ovaries. There was a solid right ovarian tumour $13 \times 10 \times 8$ cm., with a smooth, slightly lobulated surface. Its cut surface consisted of yellow-grey tissue with scattered areas of necrosis and cyst formation. Microscopy showed sheets of uniform polygonal cells with occasional microcyst formation. Mitoses were infrequent. The appearances were typically those of a granulosa cell tumour of the diffuse type (Fig. 1).

The uterus was symmetrically enlarged to pre-menopausal size and lined by thick, slightly polypoidal, endometrium. Microscopy showed cystic glandular hyperplasia of the endometrium, most of the glands showing an exaggerated oestrogen effect with marked thickening of the epithelium due to cell hyperplasia (Fig. 2).

The Registrar General has confirmed that Mrs. J.B. was born on 1st September, 1870.

# THE RESPONSIBILITIES OF THE MEDICAL PROFESSION IN THE USE OF X-RAYS AND OTHER IONIZING RADIATION

STATEMENT BY THE UNITED NATIONS SCIENTIFIC COMMITTEE ON THE EFFECTS OF ATOMIC RADIATION

## I. INTRODUCTION

1. The United Nations General Assembly, being aware of the problems in public health that are created by the developments of atomic energy, established a Scientific Committee on the Effects of Atomic Radiation. This Committee has considered that one of its most urgent tasks was to collect as much information as possible on the amount of radiation to which man is exposed today, and on the effects of this radiation. Since it has become evident that radiation due to diagnostic radiology and to radiotherapy constitutes a substantial proportion of the total radiation received by the human race, the Committee considers it desirable to draw attention to information that has been obtained on this subject.

2. Modern medicine has contributed to the control of many diseases and has substantially prolonged the span of human life. These results have depended in part on the use of radiation in the detection, diagnosis and treatment of disease. There are, however, few examples of scientific progress that are not attended by some disadvantages, however slight. It is desirable therefore to review objectively the possible present or future consequences of increased irradiation of populations which result from these medical applications of radiation.

## II. GENERAL SURVEY OF THE IRRADIATION OF HUMAN BEINGS

3. Man has always been exposed to some irradiation from natural sources. To this has now been added, as a result of modern discoveries and the applications of ionizing radiation and radioactivity, certain forms of artificial irradiation.

4. *Natural irradiation* is due to:

(1) Cosmic radiation,

(2) "Background" gamma radiation from radioactive substances present locally in the earth, rock or building materials, and from disintegration products of radon in air,

(3) Radiations emitted from natural radioelements such as potassium 40, radium, radon and carbon 14 which are incorporated in the body.

5. The amount of this natural radiation varies with locality, but has been estimated as usually delivering between 70 and 170 mrems per year to the gonads. Of this total, the major contributions are of about 45 per cent from local gamma radiations, 30 per cent from cosmic rays and 20 per cent from body potassium 40.*

6. *Artificial irradiation* is derived from:

(1) The contamination of the environment, the atmosphere, or water by radioactive waste from atomic industries or from users of radioelements;

(2) The radioactive fallout, at greater or lesser distances from the source, or radioactivity resulting from the explosion of nuclear devices;

(3) The occupational exposure of certain groups of workers: medical practitioners, radiologists, dentists, nurses, atomic energy workers, uranium or thorium miners, and the industrial or scientific users of radiation generators or radioactive isotopes;

(4) The medical use of X-rays, other ionizing radiations and radioelements in the detection, diagnosis, investigation and treatment of human diseases;

(5) The use of certain devices which emit radiation, such as television receivers, watches with luminous dials, and the X-ray generators used for the purpose of fitting shoes.

* From reports sent by India, Sweden, the United Kingdom and the United States of America.

7. The amount of artificial radiation must vary considerably in different countries and we have inadequate information as to the over-all significance of these factors. In certain countries where estimates have been made, it appears that the greatest gonad irradiation of the population is due to diagnostic radiological procedures, the amount from this source about equalling that from all natural sources in certain instances. The total present contribution from occupational exposure, from the products of atomic industries, from radiotherapy and from the radiating devices mentioned above (paragraph 6, sub-paragraph 5) is likely to be very considerably smaller. That from radioactive fallout to the gonads appears at present to be in the region of 1 per cent of the natural gonad irradiation in most areas.*

8. Both the magnitude and the significance of these various sources are under review by the Committee. Since medical irradiation accounts for a substantial, if not the major proportion of all artificial exposure, it is important that its magnitude should be known accurately for different countries and circumstances. The possibility of making such an assessment depends upon the help of the medical profession, and particularly on the adequacy and availability of records kept by doctors, dentists and organizations responsible for the use of ionizing radiation.

## III. Radiation Hazards

9. The medical use of radiation is clearly of the utmost value in the prevention, diagnosis, investigation and treatment of human disease, but the possible effects of this irradiation of individuals require examination.

10. Generally speaking, the irradiation of living beings may produce radiobiological effects either on the irradiated individual himself or, through him, on his descendants; the former being termed somatic and the latter genetic effects. Somatic effects vary according to the different organs or tissues affected, and range from slight and reversible disturbances such as cutaneous erythema to the induction of leukaemia or of other malignant diseases. The possible reversibility of the somatic effects of radiation received in small doses or at low dose rates encourages the belief that there are permissible doses of radiation which will not cause completely irreversible or significant somatic damage. The threshold for occasional somatic damage may, however, prove to be low. In the case of genetic effects, on the other hand, there may be no threshold. These effects increase with a frequency corresponding to the total amount of radiation received by the germinal tissues, and, in the great majority of cases, are adverse.

11. Many other factors complicate the interpretation of radiobiological effects. The differences between whole and partial body radiation, between a single exposure and continuous irradiation, or between the effects of different types of radiation are still imperfectly understood. Biological differences in the radiosensitivity of various tissues, or of the tissues of people of different age or sex, obviously influence the nature of radiation hazards. It is clear, however, that any radiation of gonads, and any substantial irradiation of other tissues, involve a chance of significant damage which requires assessment.

## IV. General Recommendations Regarding the Medical and Occupational Irradiation of Human Beings

12. The Radiological Profession, through the International Commission on Radiological Protection,† has undertaken a valuable and responsible duty in defining maximum permissible limits of exposure for the main radiation hazards.

13. The establishment of these maximum permissible levels for those who are occupationally exposed to radiation depends on the view that there are doses which, in the light of our present knowledge, do not cause detectable somatic injury in the individual irradiated; and on the consideration that the number of individuals concerned is small enough for the

* According to the reports sent by the United Kingdom and the United States of America.

† See the report of the International Commission on Radiological Protection, published in the *British Journal of Radiology*—Supplement 6, of December, 1954, in the *Journal Français d'electro-radiologie*—No. 10, of October, 1955, etc.

genetic effects on the whole population to be negligible. For the gonads, or for irradiation of the whole body, the levels are such as to exclude doses greater than 0·3 rem in any week or 3·0 rem in any 13 weeks, or a sustained irradiation rate greater than 5 rem per year. These values imply that no total dose of over 50 rem will have been received by the gonads by the age of 30, or of over 200 rem by the whole body by the age of 60, in any occupationally exposed person.*

As regards irradiation of the whole population, it is considered prudent to limit the average dose to germinal tissues from artificial sources to the order of magnitude of that received from all natural sources.

14. In considering the extent to which the population is irradiated for medical purposes, it is essentially the genetic hazard which is involved although it seems possible that in certain circumstances somatic injury may occur occasionally after low doses of radiation arise. Otherwise, the relevant dose is that indicating the mean gonad irradiation among the population as a whole up to the end of the average reproductive period.

15. The extent of such genetic irradiation from diagnostic procedures has been found to be equal to at least 100 per cent of all natural radiation in two countries,† and that from a third equalled at least 22 per cent of this figure.‡ Even before obtaining more exact values for these and other countries, it is clear that the exposure can be substantial in countries with extensive medical facilities, and that it is essential to consider any ways in which this exposure could be reduced without detriment to the existing or developing value of medical radiology.

16. The Committee is therefore anxious to obtain the help of radiologists in suggesting through appropriate governmental channels any methods by which this total exposure could be reduced and in estimating the amount of reduction that might be expected from any such methods. In particular it would be valuable to know how much the radiation to the gonads could be reduced:

(*a*) by improved design or shielding of equipment,

(*b*) by fuller training of any individuals using radiographic or fluoroscopic equipment,

(*c*) by any local shielding of the gonads that is practicable, especially during abdominal or pelvic examination,

(*d*) by the use of techniques involving radiography rather than fluoroscopy when full information can be obtained by this means,

(*e*) by improvement of administrative arrangements designed to obviate unnecessary repetition of identical examinations of the same subject,

(*f*) by a general study of certain medical conditions such as that of peptic ulcers, to identify the circumstances in which the establishment of a radiological diagnosis has or has not a definite influence upon the treatment or prognosis given.

## VI. Summary

(1) The Scientific Committee on the Effects of Atomic Radiation established by the United Nations General Assembly accepts the view that the irradiation of human beings, and especially of their germinal tissue, has certain undesirable effects.

(2) Information received so far indicates that, in certain countries (Sweden, United Kingdom, United States of America), by far the most important artificial source of such irradiation is the use of radiological methods of diagnosis and that this may be equal in importance to radiation from all natural sources. It is possible that such radiation may be having a significant genetic effect on the population as a whole.

(3) The Committee is fully aware of the importance and value of the medical use of radiations but wishes to draw the attention of the medical profession to these facts and to the need for a more accurate estimate of the amount of exposure from this source. The help of the medical profession would be most valuable to

* See the report of the International Commission on Radiological Protection, published in the *British Journal of Radiology*—Supplement 6, of December, 1954, in the *Journal Français d'electro-radiologie*—No. 10, of October, 1955, etc.

† Sweden, United States of America.

‡ United Kingdom.

make it possible to obtain fuller information on this subject.

(4) The Committee would be particularly grateful for information through appropriate governmental channels on ways in which the medical irradiation of the population can be reduced without diminishing the true value of radiology in diagnosis or treatment.

# CUTHBERT LOCKYER

*A Tribute on the Occasion of his Ninetieth Birthday*

In writing this short tribute, I would first pay homage to the man, and then to his work. Cuthbert Lockyer is a great English gentleman, and that briefly summarizes his character. There is a deep religious strain of Christian belief, very evident and not concealed beneath the surface: an intention of service to his fellow men, women and, one might add, children (for he was a keen member of the Marylebone Scout Association until his retirement).

A deep love of the Arts was part of his character. He was a lyric tenor and keenness for singing was maintained by a beautiful voice well trained (for he found time to engage in singing lessons to the very end of his active career).

The enjoyment he obtained from painting was great and this love determined the time and the place of his vacations. Visits to Italy, the Yorkshire dales or Scottish moors were all arranged with the object of painting the beautiful. The style was modern rather than classical. He was a regular exhibitor in medical art displays.

Of his sporting activities in younger life I do not know, but from middle age onwards he was a rather indifferent golfer, albeit a regular attendant at the practice nets working under the tuition of a well-known golfing coach.

He had a delightful home in one of the large old-fashioned types of house in Harley Street with a basement kitchen and a roof garden. In it he had a laboratory. This introduces the professional side of his life. After his first-born, his wife became an invalid and he cut down much of the social side of his life to be with the woman he so dearly loved. This, I believe, was the reason for the laboratory in his home. As a gynaecologist he was pre-eminent in several directions. Assuredly in his day he was the foremost gynaecological pathologist among the English speaking and specimens and microscopical slides of doubt or obscurity were referred for his masterly pronouncements. This work culminated in the formation of the Lockyer collection of museum pieces. It is still the finest collection in Britain though other teaching schools are now following in the steps of the Master.

Cuthbert Lockyer was a son of Charing Cross Hospital and, without fear of contradiction, it can be said its most distinguished son. Yet his appointment to the hospital staff was a matter of sharp controversy at the time. Unanimously recommended to the vacancy on the staff by the Medical Committee, the Governing Body were attracted by the young Edinburgh graduate who had just been appointed to the staff of the Chelsea Women's Hospital. To the consternation of the Medical Staff they gave the vacancy to the young Watts Eden. The reaction of his medical colleagues was to make a new appointment, viz., that of Tutor, to which C.L. was elected and this position he held for many years together with his appointment to the Samaritan and Royal Northern Hospitals. In spite of this initial handicap a great international reputation was soon established. Reference has been made to this incident because of the interest to, and possible bearing it may prove to have, on the younger generation faced with the frustrations and difficulties which exist in the profession at the present day. It is a fine example of what can be achieved in face of difficulty.

As a surgeon, although accomplished as an abdominal operator, it will be for his vaginal surgery that his fame was established. A long study at Bonn had produced a mastery of the vaginal approach in which he excelled. The Lockyer collection contains many specimens which are a tribute to his skill in this direction. As a diagnostician his accuracy was amazing. His case notes were careful and meticulous and he looked for the same high standard in those who worked with him.

CUTHBERT LOCKYER

As a teacher there are others who have greater gifts, but as a writer he was clear and lucid in style with a definite bias in the direction of pathology. His one great creation *Fibroids and Allied Tumours* is as up to date today as when it was written, and, although it never reached a 2nd edition, there was no occasion—it required neither alteration nor amendment. Incidentally many of the illustrations are from his own pen.

The text-book of *Gynaecology* or "The Red Book" as he always called it himself, is better known and has been through several editions. It has been modified and enlarged yet it still contains much from his original pen. The co-author Watts Eden had long before this time become his great friend. Those who knew both men well have no difficulty in distinguishing the contributions of either author. The senior author wrote in a rather more fluent style, but the partnership was perfect.

Finally a word about his friends. He was a much travelled man and had visited many foreign clinics. Among his distinguished foreign friends mention should be made of Wertheim and of Stroganoff. With Wertheim, he performed the first Wertheim operation in Great Britain. The specimen is in the Lockyer Collection, carefully kept because of its historic interest. To the many who still do not know, it illustrates what a Wertheim operation really is (and what it is not). Mention of the name of Stroganoff brings forward one final point—C.L. was not an obstetrician. In the evening of his professional life, Charing Cross Hospital acquired an Obstetric Ward for the first time but he played little active part in the conduct or management of cases. I always suspected that he enjoyed performing Caesarean section, albeit infrequently, for the reason given.

Not long before his retirement his wife passed on. In the course of time he contracted a second marriage and to Dr. Lockyer and to Mrs. Lockyer we wish many years of happiness —in their delightful home in Cornwall—and a happy ninetieth birthday to the grand old man himself.

EVERARD WILLIAMS.

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## ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

A MEETING of Council was held in the College House on Saturday, 23rd March, 1957, with the President, Sir Charles Read, in the Chair.

Mr. J. B. Blaikley was appointed to visit New Zealand and Australia and Professor T. N. A. Jeffcoate was appointed to visit Canada and the Caribbean area both as Sims-Black Travelling Professors. The visits will be made in 1958.

# THE LIBRARY OF THE ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS DOWN TO THE YEAR 1850

BY

SIR EARDLEY HOLLAND

ALL members of the College will be pleased that, at last, a Catalogue of the library has appeared; for now they can know what books are on the shelves and, even more important, they are made aware of those that are not. Now that the library's "wants" have been openly proclaimed, those who could help to supply them may feel the urge to do so by gift or bequest.

This is a short title "Catalogue of the Library up to 1850"; it lists about 620 books and was prepared by the consultant Librarian to the College, the well-known Mr. W. J. Bishop, formerly of the Wellcome Historical Library and now Librarian to the British Medical Association.

## THE FOUNDING OF THE LIBRARY

The origin of all libraries of historical books is interesting. This library came into being in the year 1932, when Professor William Blair Bell, the first President of the College and its greatest benefactor, presented the house in Queen Anne Street. Realizing, too, that an historical library would be its essential cultural centre he gave, and took a hand in designing, the fine suite of mahogany bookshelves that line its walls. He gave, moreover, many books from his own collection and appealed to those members who had old midwifery books to do the same. In those early years many young gynaecologists had begun to collect, inspired, no doubt, by the example and writings of Herbert Spencer, Lloyd Roberts, Ballantyne, and other seniors, and by the young Professor Miles Phillips. Besides, in those days, old midwifery books abounded and could be bought for a tithe of their present price. For the last 20 years or so they have become progressively scarcer and more costly, so strong has been the drift to wealthier countries with well-endowed libraries.

The nucleus of the library was the collection of some 450 books bequeathed by the first President. His collection was essentially the working library of an unusually active researcher, practitioner, teacher and writer, and hence contained many modern books on obstetrics, gynaecology and physiology. It also contained the all but complete works of the renowned Edinburgh surgeons, Sir Charles and John Bell, who were his kin. The antique midwifery books (no doubt depleted by his original gift to the library) were not more than some 10 per cent of the whole, but amongst them were eight copies of Roesslin's *Birth of Mankinde*, Rhodion's *De partu hominis* (1532 Ed.), Rueff's *De Conceptu* (1580 Ed.), copies of Harvey's *Exercitationes de generatione*, and the scarce first edition of Chas. White's *Treatise*.

In 1938 the College was enormously enriched by the acquisition of the remarkable collection of Professor Roy Dobbin (formerly professor of obstetrics in the Cairo Medical School). The College was able to acquire his collection through the kindness of Lady Simson, who gave to the College for the purpose of buying the collection the sum of £500 collected by some of the patients of her late husband, Sir Henry Simson, to found a memorial to him. The executors of Roy Dobbin also were generous, for this sum was only a token price for a collection of books many of which were very scarce and all in perfect condition.

Dobbin chose to live a quiet life, was a scholar and a linguist who could read his books in Latin, French, Italian, German and Arabic as well as in English, and was one of those rare people, a true bibliophile. It is surprising that

anyone living so remote from the bookshops and auction rooms of the western Capitals could make such a collection. One of the most interesting and revealing books in the collection is his own loose leaf catalogue in which, in his exquisite script he lovingly described his books with scholarly enthusiasm. Should not a photostatic copy of this revealing bibliophilic document be made for the library? It would be of absorbing interest to all book-lovers. The introduction is interesting: "These books were shown in the library of the Kasr el Any Hospital, Cairo, on the occasion of the centenary of the School of Medicine. The date was 1928. The books were exposed in the jewel cases of the Tutenkhamen Treasures Museum . . . for three weeks, seven cases in all. An attempt to burst into the largest and strongest of the cases a day before the exhibition fortunately did not succeed. The Chief of Police put a special man on duty to watch the cases for the remainder of the time."

The collection numbered some 130 books of which only about 20 are non-midwifery; but these are all treasures and include the early works of Estienne, Servetus, Spigelius, Vesalius, and a noble folio of Jacques Guillemeau's *Oeuvres*. Amongst the midwifery books, most of the choicest from Roesslin to the eighteenth century writers are in it; and there are some books seldom listed in libraries, amongst which may be mentioned three that have to do with early Caesarean section: F. E. Cangiarmilia (1758), R. Castro (1689), J. Primrose (1653), and the now scarce writings of the famous French midwife, Loyse de Bourgeois, complete except for those to do with the controversial death in childbirth of her patient, the Duchess of Orleans (1627), and the book with the first coloured plates used in a midwifery work by the 18th century French midwife, Le Boursier du Coudray.

Coming now to the College library, the catalogue shows a choice, though far from complete, collection of pre-1850 books. One naturally turns first to Roesslin's *Birth of Mankinde* and its precursors. Of Roesslin's *Rosengarten* (the oldest book on midwifery printed in the vernacular) there is a clean and perfect copy of the 1532 edition. There is also a copy of Gustav Mann's facsimile of the first edition (1513) which, with its history of the book and the editions, is an essential work for the student of early European midwifery. Of *De partu hominis*, the translation into Latin by Roesslin's son, the Library has three copies, two of the first (1532) and the others of the 1536 edition. It was this Latin translation that enabled the book to be translated into other languages—English, French, Dutch, Spanish and Czech. Roesslin was indeed rightly called "the teacher of the midwives of Europe". Of the 20 editions of the *Birth of Mankinde* the Library has 8 (9 copies), thus coming a good second to the Royal College of Physicians of London which has 15 copies (11 editions), eleven of which, including two of the scarce first edition (1540), came from the Lloyd Roberts bequest. But the College collection is nevertheless a notable one; most of the copies are in fine condition, that of the 1545 (second) edition being a beautiful book, in almost mint state.

### The Post-Roesslin Period

About the middle of the seventeenth century the *Rosengarten* and its translations ceased to be the universal textbooks and were supplanted by the more scientific midwifery books of surgeons who had learnt by clinical observation and made their own inferences instead of adhering to the ancient teachings. During the early part of this period (the late 17th and early 18th centuries) the centre of publication of works on midwifery, with the notable exceptions of those of Harvey and Deventer, was Paris, and the names that stand out most are J. Guillemeau, *De la Grossesse et Accouchemens* (1620), Mauriceau, *Des maladies des Femmes Grosses et Accouchées* (1668), Paul Portal, *La pratique des Accouchemens* (1685), Phillipe Peu, *La pratique des Accouchemens* (1694), P. Dionis, *Traité général des Accouchemens* (1718), La Motte, *Traité complet des Accouchemens* (1722) and the two famous midwives Loyse de Bourgeois (whose books have already been mentioned), and Mme du Tertis, also known as La Marche, who wrote two books for the instruction of midwives (1677 and 1710). Thanks to the Dobbin collection the works of these authors are well represented in the Library, the

only notable absentees being Mauriceau's *Aphorisms* (1694) and *Observations* (1695).

The Library has three copies of Wm. Harvey's *De generatione* (1631) and one copy of the first English translation (1656). Two other rarities are the text book for midwives (1690) by the famous German midwife Justine Siegemundin, and *Speculum matricis or The Expert Midwives' handmaid* (1671), the earliest book for midwives written in English, though by a Cork physician, J. Wolveridge. Of Deventer's famous *Novum Lumen* (1701), there are only late editions and the French and English (*The art of midwifery improved*) translations. It is to be hoped that the Library may one day acquire a copy of P. Willughby's *Observations on Midwifery*, of which only 17 copies are known to Professor Miles Phillips; though the manuscript was not discovered and published until 1863, much of it must have been composed during his long period of friendship with Wm. Harvey and should be listed with these early books.

### The Pre-Smellie Period

During, approximately, the second quarter of the 18th century, the notable British authors were John Maubray, John Manningham, Edward Chapman, Fielding Ould, B. Exton, Wm. Gifford, G. Counsell and J. Burton. Most of these are well represented in their first editions, but noticeable absentees are: Maubray's rarer work, *Midwifery brought to perfection* (1725), in which as a teacher he appealed for the establishment in London of a lying-in hospital on the lines of the Hotel Dieu in Paris; Ould's *Treatise* (1742), an important book and not hard to acquire, and Counsell's *The Art of Midwifery and the Midwives' sure guide* (1752) in which he suggested that "all midwives and midmen" in the London area should after a period of apprenticeship be examined by the Royal College of Physicians.

The most important book of this period undoubtedly was Chapman's *Treatise on the improvement of Midwifery* (1733) in which he described his forceps, a great improvement on those of Chamberlen and Dussé. The Library has only the second and third editions of this epochal book of which it is said, with truth, that it gave a great impetus to British midwifery and encouraged British obstetricians to write books. Indeed, Glaister asserts that "the centre of publication of works on midwifery was changed from Paris to London" and "the chief advancements in the science of midwifery were made by British Obstetricians".*

### William Smellie and His Circle

In 1739 Smellie, 42 years old and much experienced in midwifery, settled in London, where he found as colleagues, Chapman, Manningham, Exton, Harvie, R. W. Johnson, and the young Leake and Wm. Hunter (who lived with Smellie for a time). These were the men who, led by Chapman, were beginning to make London Europe's chief obstetric centre, a process to the furtherance of which Smellie soon began to add his great gifts. When he left London twenty years after his arrival he had become the most popular teacher, the most reputed practitioner and the most famous writer, as well as having won a European reputation.

All Smellie's works in all editions should be in the Library. In 1751/52 he published Volume I of his *Treatise on the Theory and Practice of Midwifery*, which went through nine editions of which the Library has six, including the first. Volume II was published in 1754 and went through seven editions, four of which are in the Library but not the first. Volume III was published in 1764, one year after his death, and had six editions, of which five, including the first, are in the Library. So the Library's assemblage of these books is nigh complete. The special Dublin duodecimo of 1764/65 would be an acquisition.

Of the *Anatomical Tables* the only edition in the Library is the first (1754), which is, of course, the most desirable and, as only 100 copies were printed, the most rare. In 1761 there was a reprint. The elephant folio edition of 1787, the last printing from the original plates, with an additional plate of Dr. T. Young's short curved forceps, was edited by Professor Alexander Hamilton. It is a book well worth acquiring. The preface tells how the copper plates, stained

* John Glaister, M.D., "Dr. William Smellie and his friends". Glasgow, 1894, p. 158.

with sea water, came into the Editor's hands after a long search and just in time to escape being melted down by a copper-smith. The octavo edition of 1785, with two extra plates by Drs. Young and Evans of Edinburgh, is interesting and rare because it was a failure as the plates were too small to be useful.

The two German-Latin folio editions, *Tabulae anatomicae—Sammlung Anatomischen Tafeln*, translated by Dr. George Huth, with 39 plates copied and re-engraved from the originals and printed in Nuremberg in 1758 and 1789, are beautiful examples of the printers' and engravers' art. They should certainly be acquired.

### From Smellie to 1800

The good rules of practice established by Smellie and his contemporaries were worthily carried on by a succession of men too numerous to name here. Up to the end of the century those that stand out most are Wm. Hunter, Leake, Charles White and Wm. Hull of Manchester, W. Aitken, W. Lowden, Alexander Hamilton of Edinburgh, R. W. Johnson, W. Perfect, T. Denman, and E. Rigby (senior), some of whom (e.g., Rigby, Hamilton and Denman) carried on well into the nineteenth century. The Library has a good selection of their writings, but there are many gaps to be filled, among them being C. White's *Enquiry into the swelling in one or both extremities which sometimes happens to lying-in women* (1788), John Aitken's *Principles of Midwifery* (1786) with his suggestion of "pelvitomy" (the forecast of the modern operation of pubiotomy) and W. Perfect's *Cases in Midwifery* (1783). Denman's writings are complete but for a few trifles, and include the splendid quarto, with plates (5th Edition) of *An Introduction to the Practice of Midwifery*. But Volume I of the first edition of this book (1788) is wanting. Under "Edward Rigby" no distinction is made in the catalogue between father and son: the father, with his famous *Essay on the uterine haemorrhage which precedes the delivery of the full-grown foetus*, which he published when 29 years old and of which the Library lacks the first edition (1771), and the less famous son who succeeded to the fashionable practice of Sir Charles Locock (first physician-accoucheur to Queen Victoria, 1840) and wrote an unimportant *System of Midwifery* (1844). It would be interesting to acquire some of the books of Edward Rigby (senior) on general medicine to show his remarkable versatility; the writer would choose above all his *Essay on the production of animal heat and its application in the treatment of cutaneous eruptions* (1785).

### 1800 to 1850

It is no doubt artificial to make this abrupt division between the eighteenth and the following half-century. Many of the books published in the late eighteenth century ran into new editions in the early nineteenth, examples of which, as already mentioned, were those of Denman and Edward Rigby (senior). Indeed, Rigby's 6th Edition (in the Library) of the *Essay* (1822), published the year after he died, has greater interest than other editions because it contains a memoir of his life and work.

Of the new men (those who *began* to publish in the new century), there is a large number—among whom may be mentioned: James Barlow of Blackburn (whose portrait hangs in the College), who reputedly did the first successful Caesarean section in England in 1793 and described it in his *Essays in Surgery and Midwifery* (1822), James Blundell, John Burns of Glasgow, Fleetwood Churchill, C. M. Clarke, David Davis, A. B. Granville, R. Gooch, Marshall Hall, James Hamilton of Edinburgh, W. F. Montgomery and R. Collins of Dublin, S. Merriman, John Ramsbotham and his son Francis, George Spratt with his remarkable dissection colour-plates, and the great J. Y. Simpson, who, though only 38 years old in 1850, had been the Edinburgh Professor for 11 years, and had published his famous papers on the use of ether and chloroform in midwifery in the *Monthly Journal of Medical Science*; the pamphlet on the use of ether is in the Library, as doubtless is the three-volume edition of his complete works (Edinburgh, 1871).

The books of all these men are almost completely represented in the Library. The only noticeable gaps are John Ramsbotham's *Practical observations on midwifery* (1821), Marshall Hall's *Commentaries on some of the more important of the diseases of Females*, 1827, and Blundell's *Researches physiological and*

*pathological*, 1825, which is not a gynaecological book but should be acquired for the Library because it shows that Blundell was not only great as an obstetrician but also as an experimental physiologist; in it he describes his experiments on intravenous blood transfusion in dogs, and describes also six cases in which he gave blood transfusions to patients in Guy's Hospital.

### Midwives

The catalogue lists no books by English midwives, though the books of the great French midwives, L. Bourgeois, du Coudray, La Marche, Boivin and Lachapelle, and of the German midwife, J. Siegemundin, are all in the Library. At this period the French midwives were a long way ahead of the English, for the very good reason that in France, as in other European countries, schools for midwives had been founded: in Paris, the *Maternité*, with *sage-femmes en chef*, like Mme Boivin and Mme Lachapelle, and with obstetricians such as Professor Baudeloque as teachers.

The writer has only three of the five books by English midwives: Jane Sharp's *The complete midwives' companion*, 1671; Sarah Stone's *A complete practice of midwifery*, 1757, and Elizabeth Nichell's *Professed midwife*, 1760, in which she exuberantly attacks Wm. Smellie. He also has two pamphlets by the remarkable Eliz. Cellior ("the popish midwife"), one of which is only of political interest (a defence against the accusation of being concerned in the "Meal-tub Plot" against the life of King Charles II) and the other of great midwifery interest, *To Dr. —, an answer to his queries concerning the Colledg of Midwives*, 1687, her retort to a doctor who had criticized her proposal to James II for "a scheme for the foundation of a Royal Hospital for the maintenance of a corporation of skilful midwives". The books of the two other midwife authors—Margaret Steven's *Domestic Midwife* (1795) and Martha Mear's *The pupil of Nature* (1797) seem to be exceptionally difficult to find.

Though none of these women was in the same class as the Paris midwives mentioned above, their writings and personalities are of historical importance in the slow evolution of British midwives to their present high status.

Moreover, still on the subject of midwives, the catalogue lists none of those books or pamphlets directed against "man-midwifery". The ire of the midwives was first aroused when the obstetric forceps came into general use and put in the hands of the doctors a revolutionary means of coping with prolonged and difficult labours. Mrs. Nihell attacked, on the ground that man-midwifery often brought about injury or death of the baby. When this line of attack failed as, in due course it was bound to, the ground was shifted to the "immodesty" or "immorality" of man-midwifery, though this objection was raised much more by certain lay people than, to their credit, by the midwives. But at least one doctor lent his weight—Philip Thicknesse, *Man-midwifery analyzed; or that indecent and unnecessary practice detected and exposed* (1790). Many such pamphlets or books were published; the latest in the writer's collection is dated 1838, *Junonesia: or women rescued.*

### Future Policy

The preface of the Catalogue states that "It has for many years been the policy of the Library Committee to make the historical collection as complete as possible within its special field". A very laudable intention: but, having seen the lists of books in the Blair Bell and Roy Dobbin collections, and knowing a good deal about the books given by members when the Library was founded, I am inclined to wonder whether the expression "as complete as possible" may not be an overstatement. The Library, over the years, has done pretty well, but not nearly well enough considering its strong beginning.

The present honorary Librarian, Mr. A. J. McNair, must be congratulated on bringing a new zest and, above all, on bringing about the publication of this Catalogue, thus taking the first step in overcoming the apathy that seems to have bedevilled the Library for so many years and which has been responsible for the large number of gaps that still wait to be filled. It is, of course, hoped that the catalogue will result in a number of gifts, but too much reliance should not be placed on this source of supply, for the number of private collectors is now small. A dynamic buying policy should not be

delayed any longer. The buying of this sort of books is an emergency operation; constant vigilance, alertness, a swift pounce and a ruthless competition with other collectors in the field are essential. There is only one person who could do it—the honorary Librarian; the rules of the game are simple enough and the writer hopes he will be forgiven, as an old hand, for stating them. The first thing he must do is to become personally acquainted with the appropriate London dealers and give them a copy of the Library catalogue as well as a separate list of the most pressing "wants". He should call on them at intervals to maintain their interest and ensure that they are giving him the first refusals and, moreover, a casual visit will often result in an acquisition. They all send out catalogues from time to time and these must be sent to him direct. When a catalogue arrives he must at once scrutinize it and, if he sees anything likely, he must at once telephone, telegraph or call to make sure of his prey. Having secured it he may be able at once to decide to buy it, or may first take it away to collate it himself or consult Mr. Bishop, or failing his presence, the Librarian of another of the medical libraries, any of whom he would find most pleased to help him. (If he decided to buy it he would, if possible, confer with the President who would invariably, trusting the good judgment of his librarians, tell him to do so.) As London is one of the most important auction centres in the world for antique books, he would arrange to have auction catalogues sent to him direct. This is a more leisurely method of buying, for there is ample time for inspection. Lastly, there are agents whose business it is to receive and scan British and Continental catalogues and report to their clients.

It will be said that an energetic buying policy would be expensive. So, indeed it would. As the writer is finishing this review there lies on his desk a recent catalogue from a bookseller not a half mile from the College; it lists two glaring gaps in the College collection: Rueff's *De conceptu et generatione hominis* (1554), price £75, and Fielding Ould's *Treatise on Midwifery* (1742), price £40; both very scarce, both costly, both likely to double in price as the years pass.

The Council of the College must make up its mind now whether to form an historical collection or forever hold its hand. Any collector's advice would be to buy while the going is still as good as it is. The writer believes there is a library book-buying fund that could fill a good many gaps. But what about a greater sum that is lying idle on the book shelves? What about Vesalius, Servetus, Spigelius, Estienne, Mondino and a number of other books listed in the catalogue but not "within its special field"? Would not the right policy be to sell them all and put the money into the book-buying fund —and spend it?

# Obituary

# RUFUS C. THOMAS

F.R.C.S.Ed., F.R.C.O.G.

RUFUS CLIFFORD THOMAS, Emeritus Consulting Obstetrician and Gynaecologist in the Bromley Group, died suddenly at his home in Croydon on the 11th January at the age of 67.

Born at Llantwit Vardre near Pontypridd, he was educated at Christ College, Brecon, where he excelled at athletics, and studied medicine at University College, Cardiff and the Westminster Hospital. There he had the unusual experience of acting as Resident Obstetric Assistant before qualifying in 1915: after serving as Senior House Surgeon at the same hospital he joined the R.A.M.C. and saw active service in France.

After the war he went into practice in Newport where he held appointments as Honorary Anaesthetist at the Royal Gwent Hospital, Consulting Surgeon to the Maternity and Child Welfare Clinic and Consulting Gynaecologist to the Borough Council, and in 1924 was elected F.R.C.S.Ed.

In 1927 he went to India as Chief Medical Adviser to the Maharajah Jamsaheb of Nawangar and during his six years there his work, though mainly surgical, included public health work, administration of the medical services of the State and the breaking down of superstitious and religious barriers to progress. He also built a hospital and laughingly admitted that he held the rank of honorary colonel in the "Ranji's" army. He had many interesting tales to tell of the medical problems he met there, for the Purdah system prevailed, and of the hunting and shooting expeditions in which he took part. On one occasion his first task, on arriving at a village on one of his regular tours, was to organize a party to track down and shoot a man-eating tiger, which had been preying on the local inhabitants; thereafter he was at liberty to proceed with his medical duties.

In 1933 ill health forced him to return to England. After his recovery he went as Resident Surgeon to West Middlesex County Hospital and was elected a Member of the Royal College of Obstetricians and Gynaecologists in 1934. The following year he was appointed Consultant Obstetrician and Gynaecologist to the County Borough of Croydon where he did sterling work, and while there published many papers about his experiences with spinal anaesthesia, of which he was a keen protagonist. He remained in Croydon throughout the second World War, working with a much depleted staff, and in 1946 took a similar post with the Kent County Council, with headquarters at Farnborough, and was elected to the Fellowship in 1947.

With the advent of the National Health Service he remained a full-time officer, took a leading part in the formation of the Association of Whole-time Salaried Specialists and was elected President. In addition to clinical work he was a militant member of many medical and administrative committees and continued as such after his enforced retirement in 1954.

For many years he was a lecturer and examiner for the Central Midwives Board and after his election to the Fellowship acted as a member of the Council of the College, of its Hospital Recognition Committee and as an examiner for the Diploma.

In spite of his many professional duties he found time to play golf regularly and in 1955 was elected Captain of his Club, playing to a handicap of 2; he was also a very keen trout fisherman.

A man of many parts and much experience, Thomas was always ready to give advice to his younger colleagues. He will be sadly missed at Farnborough, particularly by those of us whom he helped along the road and who were fortunate enough to enjoy his friendship.

KENNETH G. SEAGER.

RUFUS C. THOMAS

# REPORTS OF SOCIETIES

## NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

### October 1956

A meeting of the North of England Obstetrical and Gynaecological Society was held in Manchester on Friday, 19th October, 1956. The President, Mr. C. H. Walsh, was in the Chair.

Mr. B. Williams presented a case record

### The Formation of an Artificial Vagina by Frank's Method

(This article appears on page 241 of this issue)

*Discussion*

The President had no personal experience of this method, but he had seen a vagina formed by natural forces. He thought Frank's method would be possible only if there was already a small depression, and that it depended on the looseness of the tissues in that area. Before treatment was begun, the patient's outlook must be considered.

Professor C. S. Russell questioned that Frank's method was the most speedy. Though the mould must be worn for 6 to 9 months, it was removed and replaced after 1 week, and the immediate treatment by McIndoe's method was 3 weeks.

Dr. R. Newton also raised this point, and thought that in 2 weeks both mould and catheter could be removed.

Mr. L. B. Patrick stressed that in McIndoe's method the mould must be used for 9 months.

Mr. W. Calvert recounted the cautionary story of a frightened girl of 17. Her original complaint was amenorrhoea, and when examined under anaesthetic no vagina was found. An artificial vagina was created, and later at laparotomy the ovaries and tubes were found, but nothing more. She returned 2 years later when contemplating marriage, the artificial vagina was increased in length, and dilators were then employed making a vagina 4 inches long. At her final visit she was very upset and had now refused marriage because of all this unpleasantness.

In reply, Mr. Williams agreed that the looseness of tissues was essential. He had been quoting results from various authors for the time required for treatment by McIndoe's method.

Mr. T. F. Redman recorded a case of

### Uterine Endometriosis Following Prolonged Oestrogen Administration

Hormone imbalance, probably excess oestrogen production, plays a part in the development of endometriosis. This has been deduced from the common association of endometriosis with fibroids and endometrial hyperplasia.

The patient was seen in January, 1955, at the age of 48 with continued vaginal bleeding for 1 month. At 23 her only pregnancy ended in abortion, and that year the left ovary was removed. In 1932 the right ovary was removed, but as these operations were performed on the Continent, the reasons for them were unknown.

From 1935 to 1940 cyclic oestrogens and progesterone were given, and regular bleeding was maintained. In 1941 oestrogen implants were given at half yearly intervals, producing irregular and sometimes heavy bleeding. Since 1949, when she came to this country, she had had only 2 oestrogen implants.

The uterus was found to be bulky, and hysterectomy was, therefore, performed after freeing many adhesions. Examination of the specimen showed endometrial hyperplasia with dilated endometrial glands, and uterine endometriosis.

Mr. Redman thought that the prolonged oestrogen therapy favoured the invasion of the myometrium and stimulated the ectopic endometrium to further development. He questioned whether the adenomyosis had developed since removal of the ovaries, and thought there could have been no evidence of endometriosis at that time, but the continued growth and development were the result of oestrogenic stimulus.

*Discussion*

The President asked in what form the oestrogens were given.

Miss E. Mills observed that it was impossible to exclude ovarian endometriosis.

Mr. J. H. Malkin had known a patient with endometriosis of the recto-vaginal septum which disappeared during pregnancy.

Professor Jeffcoate found it difficult to follow the argument. It has been long established that it is difficult to grow endometriosis with absent ovaries, but this was only one factor. This patient may have been destined to develop endometriosis, and hormones had been given artificially. He mentioned Houston's report that large doses of oestrogens suppress endometriosis.

Dr. E. A. Gerrard had seen a similar condition develop after endometriectomy.

Professor C. S. Russell agreed that oestrogens were necessary for the development of endometriosis or it would occur after the menopause, but this is only one factor.

Mr. Redman in his reply said he had been trying to distinguish between the origin and continued development of endometriosis.

Mr. W. Hunter read a paper on

PREGNANCY WITH THE DEFORMED UTERUS

(This article appears on page 243 of this issue)

*Discussion*

The President thanked Mr. Hunter for his comprehensive account and commented on the scope of the discussion. He did not think there was a greater incidence of disordered uterine action.

Dr. J. K. Wilson showed slides illustrating the overall frequency of malformations. In infertility cases 38 per cent showed some often minor malformation, and in those having a normal labour at term the incidence of fundal deformity was 5 per cent. When labour was complicated the incidence rose to 29 per cent, and in premature labour 26 per cent. Arcuate and planiform types were included. Difficulty with version should make the obstetrician suspicious, also a deeply engaged presenting part with the other foetal pole in the flank.

Dr. R. Newton asked if there had been a detailed examination of all septa.

Dr. K. V. Bailey commented on the limited place of surgery. He had operated on a patient with a double uterus for dysmenorrhoea. Later she became pregnant but aborted.

Mr. L. B. Patrick had seen few difficulties in labour or the third stage from uterine abnormalities.

Dr. J. M. Gate asked if the two uterine horns contracted together or independently.

Mr. T. B. FitzGerald enquired about the value of plastic operation following repeated abortions.

Mr. C. J. K. Hamilton had reconstructed a uterus after 13 abortions and she had delivered spontaneously at the 35th week. In another case this was done after 6 abortions, and the 7th pregnancy ended in Caesarean section.

Professor Jeffcoate asked about the results of repair and risk of rupture in subsequent pregnancy. Of the 4 cases he had done, 2 went to term, 1 patient ruptured the fundus the day before Caesarean section, and the last fortunately had a placenta praevia and therefore Caesarean section. He mentioned that in some cases the uterine cavities were so small that too much endometrium could be lost at plastic operation, and menstruation was not resumed.

Mr. J. K. Malkin commented on the characteristic feel of the non-pregnant horn, when it was in the pelvis in front of the presenting part.

Mr. B. Williams mentioned the need to look out for the minor complications.

In his reply, Mr. Hunter answered many questions. He had found disordered uterine action more frequent and thought it might be due to the presence of only half the lower segment which did not dilate properly. In many cases of minor deformity diagnosis was difficult even with hysterosalpingogram. He had had few specimens to examine microscopically, and was interested in the anatomy of the recto-vesical septum.

The non-pregnant horn could be felt contracting in between the pregnant horn's contractions. The rather unsatisfactory results gave hysteroplasty a small place in the treatment of repeated abortions. The minor deformities gave rise to a high incidence of transverse lie, and he thought the optimum time to divide a vaginal septum was the middle weeks of pregnancy or early labour.

## NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

NOVEMBER 1956

A meeting of the North of England Obstetrical and Gynaecological Society was held in Sheffield on Friday, 16th November, 1956. The President, Mr. C. H. Walsh, was in the Chair.

Dr. W. A. W. Dutton reported a case of

INTERSTITIAL TUBAL PREGNANCY FOLLOWING SALPINGECTOMY ON THE SAME SIDE

Dr. Dutton had found interstitial tubal pregnancy after salpingectomy very uncommon, and only 28 cases had been recorded.

The patient, a gravida-3, was admitted as an emergency in August, 1955 with signs suggestive of an ectopic gestation, and this was confirmed at laparotomy. Treatment by expressing the mole from the ampulla was considered, but total removal of the extra-uterine portion of the right tube was performed.

In February, 1956, the patient was again admitted as an emergency. The last menstrual period on 10th January had been normal, and was followed by 6-weeks amenorrhoea. For 10 days she had had intermittent attacks of severe hypogastric pain, and after admission she complained of severe generalized abdominal pain and shoulder tip pain, and fainted.

At laparotomy the peritoneal cavity was found full of fresh blood, with bleeding from the posterior aspect of the right uterine cornua, where there was a shallow circular cavity 1 cm. across. The left ovary contained a recent corpus luteum. A wedge was excised at the right cornu and the defect closed with mattress sutures. Following blood transfusion the patient's recovery was uneventful. The ectopic gestation was confirmed by section.

Dr. Dutton discussed two features: (1) Is it ever advisable to remove an ectopic mole and leave the tube, and (2) is total excision of the extra-uterine tube radical enough? In favour of this more radical measure, the risk of interstitial pregnancy is avoided, and the technique is not difficult, but the uterus is left with a scar.

*Discussion*

The President had never had the courage to express a mole because of the risk of continued haemorrhage. He advised against excision of the cornu of the uterus, but buried the cut end of the tube.

Mr. N. L. Edwards had reported a case in 1933 of internal migration of the ovum. The ampulla of the left tube was blocked and buried in adhesion, an inter-

stitial pregnancy developed, and the corpus luteum was in the contralateral ovary.

Mr. D. W. Currie, when sterilizing a patient, excised the tube and buried the stump. One patient later became pregnant, but, even after hysterectomy and microscopical examination, he did not know how this had arisen. In 27 cases he had removed portions of damaged tube leaving nylon in the lumen, and 2 of these patients had had ectopic pregnancies.

Mr. J. B. Cochrane had removed an ectopic mole by expressing it or incising the tube in 28 cases, the tube being later found patent by hysterosalpingography. Twelve patients had become pregnant, and only 1 had an ectopic pregnancy.

In his reply, Dr. Dutton remarked on the paucity of references to internal migration of the ovum.

Dr. R. L. Lunt gave a paper on

### Subarachnoid Haemorrhage in Pregnancy

Subarachnoid haemorrhage in pregnancy is rare, and Dr. Lunt had 2 cases to report.

The first, a primigravida of 28 years was seen first in the antenatal clinic. Four years previously she had sustained a subarachnoid haemorrhage which resulted in a left spastic hemiplegia. At the 26th week of pregnancy she was admitted with severe headache, followed by several epileptiform fits. She was rational but very irritable, there was some weakness of the right arm and leg, and the right eyelid drooped. Heavily blood-stained cerebrospinal fluid was removed at lumbar puncture. Retinal haemorrhages were evident in the right eye, but the left retina was normal. She died 48 hours later in spite of ligation of the right common carotid artery.

Post mortem two recent haemorrhages were found, the first in the region of the right side of the circle of Willis, and this was well organized. The other haemorrhage was in the region of the right basilar artery. On section of the brain an extensive area of yellow discoloration was found in the right cerebral hemisphere.

The second patient, a primigravida of 26 years and 39-weeks pregnant was admitted as an emergency having been found unconscious with rigid limbs. Later she regained consciousness but complained of severe frontal headache and vomiting. At first there were no neurological signs, but after 8 hours neck rigidity developed and a right extensor plantor response. Lower segment Caesarean section was considered the treatment of choice, a live child was obtained, and ultimately she was discharged from hospital after steady improvement.

Approximately 75 per cent of cases of subarachnoid haemorrhage occur as a result of rupture of an aneurysm, and the majority of these cases occur between 21 and 40 years of age, the incidence of pregnancy being that to be expected in the general population. A high percentage of cases occurred when the individual was at rest, and, of a series of 29 cases reviewed by Schwartz (1951), 19 occurred in the first 24 hours of the puerperium but only 1 in labour.

In both pregnant and non-pregnant patients 30 to 40 per cent die as the immediate result of the subarachnoid haemorrhage, and a further 20 per cent during the next 8 weeks from a recurrent haemorrhage. Any surgical treatment should, therefore, be done early.

The diagnosis of subarachnoid haemorrhage may be difficult as several conditions produce fits or loss of consciousness, but a lumbar puncture proves valuable. The management of the case from the obstetric point of view will depend on the duration of the pregnancy. If the bleeding is in the first two trimesters, any neurosurgical procedure indicated should be carried out, and after a sufficient interval vaginal delivery may be permitted after the application of forceps. Later in pregnancy Caesarean section would seem preferable, and if surgical treatment has been successful there seems no clear reason to advise against future pregnancies.

#### Reference

Schwartz, J. J. (1951): *Amer. J. Obstet. Gynec.*, **62**, 539.

*Discussion*

The President was interested because of the plea for conservative management. He understood that vaginal delivery caused a greater strain.

Mr. J. B. Cochrane had a similar problem. The patient was 24 years old, and 4 years ago a neurosurgeon had operated after a subarachnoid haemorrhage. Fifteen months ago she became pregnant and was delivered by Caesarean section. A few weeks ago she returned pregnant for the second time, and 2 days later had a further subarachnoid haemorrhage. Mr. Cochrane asked what to do now? The patient had comforted him by saying her sister had died of a similar condition.

Mr. C. J. K. Hamilton had seen 4 cases: 1 died undelivered, 2 were delivered by Caesarean section under local analgesia, and, for the last, a neurosurgeon wished to deal with the aneurysm under hibernation. What effect did this have on the baby?

In reply Mr. Lunt commented on the dramatic improvements which occur within 48 hours of Caesarean section. He preferred hypotensive drugs to hibernation.

Miss U. M. Lister and Dr. M. Buchanan read a paper on

### Foetal Distress and Neonatal Asphyxia

(This article appears on page 233 of this issue)

Part I of this paper was read at the meeting of the North of England Obstetrical and Gynaecological Society.

Mr. E. Gledhill presented

### Some Pitfalls in the Diagnosis of Foetal Distress

Mr. Gledhill outlined the main signs of foetal distress. He regarded meconium staining of the liquor as a warning to pay particular attention to the foetal heart, and, though in the majority of cases these signs are of most practical importance late in labour, the cases he proposed to describe showed signs of foetal distress in early labour.

The first case was that of a woman who already had

had one miscarriage. She was admitted in labour at term, and after 4 hours the membranes ruptured and the liquor was meconium-stained. The foetal heart 3 hours later was irregular and it was decided to deliver by Caesarean section. The baby had a spina bifida and myelocele and later died.

The second patient was pregnant for the second time. Her first child developed rubella when she was 16-weeks pregnant, and after an uneventful pregnancy she was admitted with ruptured membranes 2 weeks overdue. Meconium staining was noticed and later an irregular foetal heart. Ultimately a child was delivered with mild hydrocephalus and a spina bifida.

The third case presented a similar picture, and again a hydrocephalus and spina bifida were found.

Two other cases showed a rather different picture. The first of these patients had had 2 previous pregnancies. Labour commenced 4 weeks before term, and the foetal heart rate persisted at 48 to 60 per minute. The baby cried well at birth, but a systolic bruit was audible, and it died 50 hours later. The heart was found to be enlarged, trilocular and with a patent ductus arteriosus.

The last patient had a mitral stenosis and auricular fibrillation, but no digitalis was administered. A medical induction was given, but at the first dose of Pitocin the foetal heart rate fell to 64. Next day labour commenced after rupture of membranes, and throughout the foetal heart was under 80. The baby was healthy at birth, and only gradually did its heart rate accelerate to normal.

Mr. Gledhill asked what should be done in this type of case? The choice rests between Caesarean section and awaiting vaginal delivery, and it must be decided if it is justifiable to submit the mother to Caesarean section for the sake of a foetus which has demonstrated its inability to withstand the relatively minor stresses of early labour, and even may be gravely deformed.

*The Discussion* on these two papers was taken together.

The President agreed with the definition of foetal distress as a heart rate above 160 or below 100, fluctuations and meconium and thought it should be kept within that sphere.

Mr. H. Kramer thought an X-ray should be done before Caesarean section, and that the membranes should be ruptured to demonstrate the presence of meconium.

Mr. T. B. FitzGerald thought the two papers together were most felicitous. These signs are neglected at your peril, and the problem is to demonstrate how much they mean. Congenital deformities may sometimes be demonstrated radiologically. The methods available to analyze the phenomena of foetal distress are crude and some mechanical analysis of foetal heart sounds should be attempted.

Dr. C. J. Dewhurst commented on two points: transient foetal heart changes as the head passed through the brim, and, though he was not impressed by meconium staining, thick meconium he considered serious.

Dr. H. A. Kelsey mentioned the treatment of cases of inco-ordinate uterine action with heavy sedation and improvement in foetal heart recordings. He thought treatment should be conservative in the young fertile primigravida.

Professor C. S. Russell liked a scientific approach, but he also derived much value from the patient's decision on future management.

Mr. C. J. K. Hamilton felt the question of thick meconium or meconium-staining most important. He noticed temporary foetal heart changes on engagement of the head in early labour, and found slowing of the foetal heart during a contraction one of the earliest signs of distress.

Mr. W. S. Dickson thought that if signs of distress developed early in labour one should be loath to perform Caesarean section. In late first stage the problem is different.

Dr. D. H. Blakey commented on the oxygen saturation of cord blood showing a reduced level when there was light meconium-staining.

In reply a number of points were covered by the three speakers.

(1) The definition of foetal distress might be extended to cover lesser foetal heart changes which also carried an increased risk of asphyxia at birth.

(2) The work confirmed Mr. FitzGerald's earlier results.

(3) Transient foetal heart changes had been observed often in association with maternal distress.

(4) Temporary foetal heart slowing had not been found early in labour with descent of the head.

(5) The management often presented problems, and even after X-ray a foetal abnormality could not be excluded.

## NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

### December 1956

A Meeting of the North of England Obstetrical and Gynaecological Society was held in Liverpool on Friday, 21st December, 1956. The President, Mr. C. H. Walsh, was in the Chair.

Mr. J. Hamilton presented two case records:

### Male Dyspareunia Associated with Infertility

The patient was first seen in 1955 when she gave a history of a normal pregnancy and delivery 9 years previously. Four years later she had a missed abortion at 18-weeks maturity, and eventually the uterus was evacuated. Since that time she had noticed irregular menstruation and a discharge which persisted even after cauterization of the cervix.

Despite efforts no further pregnancy occurred, and on one occasion the husband noticed dyspareunia as from something sharp. When examined by Mr. Hamilton the patient was found to have some endocervicitis, and protruding from the internal os there was a sharp pointed object which proved to be a piece of skull bone. Curettage was done and several small bone fragments were among

the curettings. Soon after, the patient became pregnant and delivered in April, 1956.

Mr. Hamilton had been unable to find any references to a similar case. The foetus may be retained *in utero* for a considerable time, and occasionally only the bones of the foetus remain. The infertility can possibly be attributed to the presence of a foreign body and the discharge it provoked.

### An Unusual Cause of Disproportion

The second patient attended the Antenatal Clinic in 1949. Five years before she had had an arthrodesis of the right hip following a septic arthritis.

At her first examination the pelvis felt obliquely contracted, and pelvimetry was to be arranged later. When 30-weeks pregnant, the presence of twins was confirmed, but the first head was very high. Pelvimetry showed normal measurements except for the transverse which was encroached on by a Smith Petersen pin. After some hesitation the patient allowed the Smith Petersen pin to be removed as it had now served its useful purpose, and because with descent of the presenting head, severe pain was felt.

Immediately after removal of the pin the presenting head became deeply engaged in the pelvis, and two weeks before her expected date of confinement the twins were delivered.

Mr. C. H. Walsh delivered the Presidential Address on

### Sudden Death

When the dual honour of President and Treasurer had been laid upon him, Mr. Walsh had felt some trepidation at the traditions of the Society, and the thought of an address nearly made him pass out with fright. It was for this reason that he proposed "Sudden Death" as the subject of his paper.

Sudden death has been defined as the termination of life which comes quickly, under circumstances when its immediate arrival is unexpected. This definition helps to accentuate the unexpected nature of the occurrence rather than the time factor, and these cases, whether obstetrical or gynaecological, not only live in one's memory for ever, but at the time give rise to considerable anxiety, and often carry medico-legal implications. These deaths can be classified into three groups: (*a*) those associated with non-obstetrical lesions; (*b*) a combination of co-existing disease and obstetrical lesions; and (*c*) primarily obstetrical lesions. In this last group fall deaths from trauma, embolism, infection, haemorrhage, fulminating toxaemia, anaesthetic complications, and deaths of a criminal nature.

Generally sudden death is the subject of enquiry by the coroner if not of inquest, though there does not appear to be any statutory obligation on the part of a medical practitioner to notify the coroner. In the City of Liverpool, with a population of nearly 800,000 inhabitants, some 1,200 deaths in unusual circumstances are reported annually to the coroner for investigation, but what is surprising is that in the years 1953 to 1956, out of 3,978 cases reported to the Liverpool Coroner, only 15 were of an obstetrical nature. Of these 15 cases, there were 6 associated with criminal abortion, 2 deaths were due to acute medical disease in pregnancy, and 7 were primarily obstetric deaths.

In the years 1950 to 1955 inclusive, there were 44 maternal deaths among 46,055 labours at the three hospitals, Mill Road Maternity Hospital, Sefton General Hospital and Broadgreen Hospital: an incidence of 0·95 per thousand, the national rate in 1955 being 0·64 per thousand. Of these deaths 25 were due to non-obstetrical causes or a combination of factors. Into group (*a*) fall 2 cases, the first a 4th gravida admitted at the 26th week of her pregnancy with general malaise. Before a diagnosis could be established, the patient died, and a post-mortem was performed forthwith, death being found to be due to acute poliomyelitis causing bulbar paralysis. The second patient was found to have a positive Wassermann test. She collapsed 4 days after the second injection of N.A.B., had a fit and became unconscious, death ensuing a few hours later. Post-mortem findings supported a diagnosis of arsenical poisoning.

In group (*b*) there were 2 cases of sudden death. A 3rd gravida with known essential hypertension attended at the 25th week with headache, vomiting and ankle oedema. Her blood pressure was 210/140, and while admission was being arranged she complained of retro-sternal pain, her blood pressure fell to 105/85 and the foetal heart stopped. It was thought that an accidental haemorrhage had occurred but, despite treatment, death soon followed. Autopsy revealed a haemo-pericardium and a dissecting aneurysm. Rather surprisingly the kidneys proved to be completely normal. A careful review of her past obstetric history showed that in the first pregnancy all had been normal until the 36th week when a severe toxaemia developed, and there was a small accidental haemorrhage. This happened again at the 18th week of her second pregnancy. Did the first pregnancy unmask a basic hypertension, or did the toxaemia produce the hypertensive syndrome?

The second case in group (*b*) gave some difficulty in diagnosis. A primigravida was found to have a dextrocardia but her general health was good. Radiological investigation showed that the aorta descended on the left, that there was eventration of the left dome of the diaphragm, and the stomach showed a marked cardio-pyloric volvulus. At the 22nd week of pregnancy because of continuous vomiting, laparotomy was done, and gross intestinal distension was found to the middle of the transverse colon, a loop of which had slipped through a defect in the diaphragm. The patient collapsed and died 20 minutes after operation.

Of the 19 deaths of a primary obstetric nature, there were 13 which could be included in the category of a rapid nature, and concealed accidental haemorrhage was responsible for the greatest number. There were 5 cases so dramatic that treatment was unavailing, and one of these illustrates the unpredictable events.

The patient was seen regularly and all seemed normal until the 33rd week. A few days later she was admitted with classical features of accidental haemorrhage of mixed type. Dextravan was given until blood was

available, and after spontaneous delivery, despite a well contracted uterus, there was a steady trickle. Blood was administered but she died 6 hours after admission. At autopsy the blood remained fluid, and it was assumed that a coagulation defect was a factor in her death. The points to be stressed are the prior absence of toxaemia, and the management of these grave emergencies.

At Mill Road Hospital of the 84 cases of toxic accidental haemorrhage, only 19 showed earlier evidence of toxaemia, an incidence of 23 per cent. When 77 per cent of these cases are unpredictable it makes one wonder how far we have advanced in knowledge. We are now more aware of the risk of hypofibrinogenaemia, the condition may be quickly recognized, and there is evidence that the infusion of large quantities of Dextran may aggravate a blood coagulation failure, so that it would seem more logical to use double strength plasma to combat fibrinogen deficiency. In the cases where there is a steady trickle of venous blood after delivery, the uterus should be left severely alone, and shock treated by noradrenaline which sometimes has a dramatic effect, but there still remains a gross lack of knowledge of the cause of this condition.

There was one death from haemorrhage in a young healthy primigravida. After delivery the placenta was retained, and manual removal performed. Her condition appeared good, until there was sudden collapse and death despite blood transfusion. Probably this death was avoidable.

Unexpected peripheral circulatory failure occurred in 2 patients. In one, a 3rd gravida, niggling pains had occurred for 2 days prior to rupture of the membranes, and 34 hours later, though there was no temperature, the liquor became offensive. There was then a dramatic turn. She had a rigor, delivered a stillborn child, collapsed, and with increasing cyanosis, died 2½ hours later. It was thought that there was some link between intra-partum infection and the shock.

The second patient was Rh negative and antibodies were present. There was some difficulty at delivery due to foetal ascites, and a trickle of blood started. After delivery she collapsed, and was given Dextran and blood, but died 3 hours later. This case has been responsible for the introduction of the rapid thrombin test, and the restriction of Dextran.

Two patients died undelivered with fulminating eclampsia, and 2 anaesthetic deaths were reported to the coroner. One of these patients died without recovering consciousness after Caesarean section, and at autopsy a subarachnoid haemorrhage was found, and the other presented difficulty over the exact cause of death. An attempt at pudendal block was frustrated by lack of co-operation, and, during the induction of general anaesthesia, she vomited, later there was cyanosis, convulsions and death. Post-mortem showed clear air passages, and pyelonephritis in the left kidney. It seems that the lesson to be learned is that a general anaesthetic in pregnancy forms a real hazard.

The cause of death of the 13th patient in the series remains a mystery. She was a healthy primigravida, but at the 36th week an anencephalic foetus was discovered, and for this the membranes were punctured. At the completion of this procedure she lost consciousness, and despite all measures, died. The clinical features of loss of consciousness, convulsions, cyanosis and stertorous breathing suggested a diagnosis of amniotic fluid embolism, but no positive evidence of disease or significant lesion was found at post-mortem to give a logical explanation.

In cases of amniotic fluid embolism, it is postulated that the cause of death is silting up of the pulmonary vessels by the particulate content of the amniotic fluid, but in some cases where there is minimal evidence of obstruction to the pulmonary bed, it might well be that an anaphylactic reaction is the cause of death. We have yet to learn more to prevent these maternal deaths, and there is no room for satisfaction and complacency on the score that the maternal mortality rate is now at a low level.

In 1937 a patient aged 41, was anxious for investigations into the cause of her 13-years infertility. Clinical investigation revealed no obvious pathology, and under anaesthesia air insufflation was undertaken. On insufflation at a pressure of 150 mm. of mercury, air could be heard passing through the tubes, and a volume of 150 ml. was used. At this moment the patient was reported in poor condition, and within 4 minutes she died. Autopsy showed air in the uterine vein, inferior vena cava and right auricle—a lethal volume of 150 ml.

A young primigravida attended the Antenatal Clinic, and all was found normal except for a *Trichomonas vaginalis* discharge. Treatment by vaginal insufflation of an antiseptic powder was performed, and on the second occasion she collapsed and rapidly died following convulsions. Again air was found in the inferior vena cava and right auricle, and the placenta showed a small detachment at its lower border with antiseptic powder in a maternal sinus. The mechanism of death may be due to filling of the right heart with foam which is compressible but cannot be expelled, so resulting in right heart failure, but a more likely explanation is that death is due to blocking of the pulmonary artery and the arrest of the pulmonary circulation as in amniotic infusion deaths. On occasion cerebral air embolism may occur, and to explain the paradoxical embolism in the absence of an interauricular septal defect Professor Jeffcoate's note to the Society in 1954 is of significance. The knowledge that fatal air embolism may occur in the course of investigation and the treatment of patients may have considerable significance to medical jurisprudence.

Mr. P. Malpas on behalf of the Liverpool members of the Society thanked Mr. Walsh for his address, and for the care he had taken of the Society both as President and Treasurer.

Mr. J. W. Hunter (Manchester), Mr. D. W. Currie (Leeds), Mr. J. B. Cochrane (Sheffield) and Mr. W. Hunter (Newcastle) as representatives of the four other centres of the Society expressed their appreciation for the President and Treasurer.

# HOSPITAL REPORTS

BY

J. S. TOMKINSON, M.B., F.R.C.S., M.R.C.O.G.

## THE CLINICAL REPORT OF THE ROTUNDA HOSPITAL FROM 1ST NOVEMBER, 1954 TO 31ST OCTOBER, 1955

IT is difficult to do justice in a short review to this admirable report. The publication is prompt, the commentaries are instructive and the whole record is so alive that one feels one is completely *au fait* with the goings-on at the Rotunda. The various clinical and departmental chiefs write about their activities and the Master or the Assistant Master comments, generally for a paragraph or so, at the beginning of the report of each complication (which is given its corresponding R.C.O.G. table number).

During the year 4,177 women were delivered in the Intern Obstetrical Department, a decrease on the previous year as 15 beds were out of use due to extensive building taking place. Two deaths occurred in this department, the lowest recorded in the work of the hospital. The Extern Department delivered 1,560 patients, also a decrease, among whom no death occurred.

The stillbirth rate in all aspects of operative delivery was greatly reduced; for instance out of 121 cases of disproportion and contracted pelvis no stillbirths occurred and one neonatal death. The foetal loss in forceps delivery (3·4 per cent) was nearly half that of the previous year, the Master indicating that he advocates a forceps delivery at the earliest indication of foetal distress in the second stage of labour if conditions are feasible for delivery. The incidence of forceps delivery was 12·4 per cent. The incidence of Caesarean section was 4·18 per cent with a foetal loss rate of 5·8 per cent. The operation was followed by hysterectomy on one occasion for ruptured uterus, and by symphysiotomy on 2 occasions.

The Assistant Surgeon to the Rotunda Hospital contributes a page to the report on the activities of the Varicose Vein Clinic and contributes useful details about his technique. He aims at producing endosclerosis rather than thrombophlebitis, so that the endothelium, muscular and fibrous coats are firmly fibrosed and there is no clot which may re-canalize. He says "I think I have spotted the type of vein in which this result can be achieved. It must have a reasonably well-formed wall which is capable of becoming spastic and, with the help of external bandaging, of maintaining the spasm for the necessary period, i.e., six days. One cannot expect this result if the segment of the vein is so sacculated that it is incapable of going into spasm."

There is so much of interest in this report that one could continue to quote from nearly every page. It is recommended for further study.

## NATIONAL MATERNITY HOSPITAL, DUBLIN. CLINICAL REPORT BY THE MEDICAL STAFF OF THE HOSPITAL FOR THE YEAR 1955

THE commendatory review notes made above for the Rotunda Hospital apply equally well to this report of the National Maternity Hospital, Dublin. Useful commentaries precede the tables and it is interesting to compare and contrast in detail the practices at the two hospitals. For instance, information is given in the National report of 33 symphysiotomies performed during the year and an interesting 2-page commentary is given; at the Rotunda it was performed twice, combined with Caesarean section.

The Intern Maternity Service, with 132 beds available, delivered 4,885 patients, of whom 2 died. The Extern Maternity Service conducted 547 deliveries without a maternal death. The gross foetal loss rate was 3·6 per cent for forceps deliveries, performed in 11·7 per cent of deliveries over 28 weeks. To quote from the report: "Not only have the forceps increased in number, but what is significant is that they have decreased in risk, shown by a dramatic fall of over 50 per cent in foetal loss. It might be said that the foetal survival rate can be made to look impressive by 'dilution' resulting from a high proportion of easy 'lift out' forceps deliveries with of course minimal foetal risk. However, with a low section rate (1·06 per cent) it will be appreciated that a correspondingly high rate of mid-forceps deliveries is likely and that the addition of such unfavourable cases counterbalances any possible dilution with easy cases." Although in many places the dorsal position of the patient is advocated for the better definition of the foetal head and so that she need not be turned for the third stage, combined with a pudendal nerve block for complete safety for the foetus so that the hazards of the induction of a general anaesthetic are avoided, the report states that in the technique of forceps deliveries they stress that the best position for low forceps delivery is the left lateral position and that open ether is the safest anaesthetic in all hands.

This is the last report to be written during the Mastership of Dr. Arthur P. Barry. It is one of enviable success and he is to be congratulated most sincerely for his

stimulating discourses in the report and for the excellent results his teaching has produced.

## CLINICAL REPORT OF THE MATERNITY DEPARTMENT OF THE GENERAL HOSPITAL, KUALA LUMPUR, MALAYA, FOR 1955

THIS unit is the main maternity hospital for Kuala Lumpur (population about 300,000) and also acts as the central obstetric hospital for the State of Selangor (population about 850,000), for it is the only one in which abdominal operations can be performed. One hundred beds are available for antenatal and postnatal cases, with a premature baby unit of 20 beds; the total of admissions, excluding premature babies, was 6,227, and the number of deliveries was 5,265. The compiler of the report has made his own tables, derived from the tables advocated by the Royal College of Obstetricians and Gynaecologists and has provided "back-ground information" which is necessary when dealing with problems which are peculiar to that area.

The report notes a further reduction in maternal and foetal mortality; 25 maternal deaths occurred (an incidence of 4·7 per thousand) and the perinatal mortality rate was 47·9 per thousand. A lot of anaemia is seen, 209 patients being admitted with its severe forms. The report states: "In Malaya anaemia is widespread and severe. For example, the mean haemoglobin level of Indian women rubber estate labourers is about 10 g. per cent (60 per cent Haldane). This state of affairs is sharply reflected in the high incidence of anaemia amongst pregnant women, always the most susceptible group of a population." A paper published by the department in association with the Institute for Medical Research, Kuala Lumpur (*J. Obstet. Gynaec. Brit. Emp.*, 1956, 63, 409), gives details of the treatment.

Although over 80 per cent of the patients received antenatal care a lot of the seamy side of obstetrics was seen in the hospital. Eclampsia occurred in 36 cases (4 maternal deaths=11·1 per cent) with a foetal loss of 35·2 per cent. Although bromethol had been found an advance upon thiopentone, the control of patients was still unsatisfactory and phenothiazine derivatives began to be used with satisfactory results so far. Destructive operations on the foetus were necessary in 11 cases, and version in labour was done 13 times. The forceps rate for the hospital was 3·1 per cent and most of them were done with a pudendal nerve block. The Caesarean section rate was 2·3 per cent, and there were 3 hysterotomies and 2 hysterectomies for ruptured uterus.

A premature baby is defined as weighing between 1,000 g. and 2,000 g. (as the babies in general are small) and of these 78·5 per cent were discharged alive. "These good results are largely due to the care of the nursing staff."

The department is to be congratulated on publishing this report so promptly, in conditions which were difficult (as pointed out in the introduction) and for making it so interesting to review.

## CLINICAL REPORT OF THE MATERNITY DEPARTMENT OF OUR LADY OF LOURDES HOSPITAL, DROGHEDA, CO. LOUTH, FOR THE YEAR 1955

THIS department has a total of 50 beds, from which 1,409 patients were delivered during the year. Twenty-nine patients were delivered in the Extern Maternity Service. Non-booked cases accounted for 545 of the total of in-patients and the only 2 maternal deaths occurred in this group. One death was due to rupture of the uterus in labour in a woman aged 39 who had had 2 forceps deliveries; at laparotomy the foetus and placenta were free in the peritoneal cavity and a transverse tear through the lower segment, resembling a lower segment incision, was seen. A subtotal hysterectomy was rapidly performed but the patient succumbed before operation was completed. The other death was due to renal cortical necrosis in a patient aged 33 who had 6 previous pregnancies, one with pre-eclampsia at the 28th week. She was admitted at the 35th week with gross oedema and albuminuria, becoming anuric after delivery of a stillborn infant and a placenta with 28 ounces of retroplacental clot.

The forceps rate was 7·3 per cent, the Caesarean section rate 1·8 per cent and the stillbirth rate 2·9 per cent. Symphysiotomy was done in 27 cases, 3 of which were "on the way out" following Caesarean section; concerning this procedure the report states: "Experience gained in treating disproportion by this method indicates the importance of early intervention, local analgesia, and awaiting spontaneous rather than instrumental delivery. Prophylactic symphysiotomy has not been employed. A transient tendency to stress incontinence lasting for about 8 weeks following delivery is not uncommon. In all cases this underwent spontaneous cure. The patient can be told, confidently, that the condition is a temporary one."

The department is to be congratulated on producing an interesting report of a year's successful work.

# BOOK REVIEWS

"The Care of the Expectant Mother." By JOSEPHINE BARNES, M.A., D.M., M.R.C.P., F.R.C.S., F.R.C.O.G., Assistant Obstetrician and Gynaecologist, Charing Cross Hospital, London. Pp. x+270, with 57 illustrations. Pitman Medical Publishing Co., Ltd., London, 1956. Price 30*s*.

THIS handy-sized book is designed as a practical guide for all who carry out antenatal examinations. The text, in which the spirit of F. J. Browne is often manifest, is largely based on the author's routine teaching of medical students and pupil midwives. The book is in three parts, dealing respectively with normal pregnancy, abnormal pregnancy and diseases complicating pregnancy. Most of the opening chapter on anatomy and physiology might with advantage be transferred to related sections later in the book: e.g., the anatomy of the pelvis to the chapter on disproportion, and the changes in the circulatory system to the chapters on cardiovascular diseases complicating pregnancy.

Controversial statements are few, but many will not agree that, at examinations subsequent to the first but before the 32nd week, abdominal palpation is not strictly necessary "unless abdominal symptoms develop or the uterus is becoming excessively large". The latter would be difficult to detect otherwise. Maternal cardiac disease is given as an indication for the induction of premature labour in the chapter on induction but not in the section on cardiac disease in pregnancy. Strict bed-rest is more important for the cardiac patient at the 28th–32nd weeks, when the strain on the heart is greater, than at the 38th–40th weeks.

On the whole, the aim to present a simple readable and comprehensive book has been fairly well achieved, but the reader might wish for a fuller account of how to assess pelvic capacity clinically—and even how to locate the ischial spines. The chapters embodying advice to the expectant mother and detailing the maternity services and benefits in Britain are particularly useful, but the essence of the book is given in the preface: "antenatal examination requires a discipline of unremitting care and attention to detail."

"Soranus' Gynecology." Translated by OSWEI TEMKIN, M.D. Pp. xlix+258. Johns Hopkins Press. Cumberlege, London, 1956. Price 40*s*.

SORANUS wrote this work, which covers obstetrics as well as gynaecology, in the early part of the second century A.D., and his placing in medical history might be best indicated by saying that he died about the time that Galen was born. Through the works of translators and compilers his views and practices survived through the Middle Ages, but this translation, the first into English, was made from the original Greek text as edited by Ilberg. Soranus wrote with clarity and power, never concealing his disagreement with others and basing his views on clinical experience. The translation is prefaced by an introduction in which Dr. Temkin draws the background to this work with skill and lucidity.

There is so much noteworthy in the text, which includes sections on care of the newborn, that the reviewer can do no more than whet the appetite with such chapter headings as "Who Are The Best Midwives?", "Up to What Time Females Should Be Kept Virgins", "What Is The Best Time For Fruitful Intercourse?", "What Care Should Be Given Pregnant Women", "When and How To Wean The Infant", and "On Uterine Haemorrhage". Dr. Temkin and his assistants spent 7 years over this translation and the result of their labour should find a prominent place in the library of all interested in the history of their speciality and of medicine in general.

"Sexual Precocity." By HUGH JOLLY, M.A., M.D., M.R.C.P. Pp. xiii+276, with 69 figures. Blackwell Scientific Publications, Oxford, 1955. Price 50*s*.

THIS comprehensive report and analysis of 69 cases of sexual precocity studied by the author at the Hospital for Sick Children, Great Ormond Street, is published in the American style as a monograph of the American Lecture Series in Endocrinology. Nearly half the volume is devoted to a full discussion of the classification and management of the various types of precocity, while the remainder is a well documented and illustrated record of individual cases, which will appeal more to the endocrinologist than the gynaecologist.

Only children presenting signs of sexual precocity before the tenth birthday are included. They all show accelerated bone growth and early fusion of epiphyses. Mental development is not precocious and only one boy showed any interest in the opposite sex.

Three main groups of cases are recognized, namely cerebral, adrenal and gonadal. A fourth miscellaneous collection includes female pseudohermaphrodites, Albright's syndrome, premature breast development and hepatoblastoma. Most of the cases belong to the cerebral group, the majority being of constitutional or functional type, with only isolated instances due to organic cerebral disease. Cerebral precocity can be distinguished from the adrenal type by the occurrence of true puberty, namely spermatogenesis or ovulation. In the adrenal cases the gonads remain infantile.

Sexual precocity is twice as common in girls as boys. Granulosa cell tumour is a very rare cause and the author makes a plea for reserving laparotomy only for these cases where a tumour is palpable. From his reading of the literature he maintains that a mass is always palpable when precocity is due to the presence of such a tumour. If this is borne in mind many unnecessary operations can be avoided.

No treatment is indicated in constitutional precocity, but psychological handling may prove extremely difficult.

"Shaw's Text-book of Gynaecology." Revised by JOHN HOWKINS, M.D., M.S., F.R.C.S., F.R.C.O.G. Seventh edition. Pp. vii+704, with 4 coloured plates and 352 figures. J. & A. Churchill, Ltd., London, 1956. Price 32*s*. 6*d*.

THIS revised edition is dedicated to the memory of Wilfred Shaw as a tribute to a great teacher. Generations of students, past and present, can testify to the popularity of earlier editions. It is at once obvious in this seventh edition that the whole work has been revised. Those chapters dealing with tuberculosis, carcinoma of the cervix, infertility and operative techniques have been rewritten to keep abreast of recent progress. Each subject is presented in a well reasoned, interesting and acceptable form, with the chapter on carcinoma of the cervix outstanding. In the special fields of radiotherapy, venereal diseases, and contraception, the editor recruited the expert assistance of Mr. G. I. Williams, Dr. C. S. Nicol, and Dr. Sylvia Dawkins respectively.

The most apparent improvement is the introduction of many excellent new illustrations, which harmonize well with the written text. One or two appear to have been included more on their technical merit than their clinical significance.

To say that this is the best edition yet is indeed to pay tribute both to the master and his pupil. "Wilfred Shaw" is assured of a bright future in the capable hands of the present editor, who is to be complimented on his masterly execution of a difficult task.

"Synopsis of Gynecology." By R. J. CROSSEN, M.D., F.A.C.S. Fourth edition. Pp. 255, with 132 illustrations. Henry Kimpton, London, 1956. Price 40*s*.

THIS synopsis of a comprehensive and expensive volume by the same author is in popular demand in the United States of America for it provides the student with a ready reference to a wealth of information covering the whole field of gynaecology. It is, in fact, a pocket reference book worthy of the attention of postgraduate students once they have mastered the fundamentals of the subject. In value it falls short of the many excellent and inexpensive textbooks available to the British undergraduate.

"Management in Obstetrics." By ANDREW M. CLAYE, M.D., F.R.C.S., F.R.C.O.G. Second edition. Pp. x+218, with 35 figures. Oxford University Press, London, 1956. Price 18*s*.

THIS book was first published in 1948 with the object of providing the fundamentals of midwifery required by the ever decreasing number of general practitioners interested in obstetrics, to steer them through the slight hazard of the Diploma of Obstetrics examination. Since that time more and more practitioners have been doing less and less midwifery, and the examination hazard has increased, as, paradoxically, has its popularity. This new edition still provides the practitioners with a firm foundation on which to prepare for the examination and also supplies a guide to the further reading now expected of him. Undergraduate students will profit from an acquaintance with this pocket volume, but the serious student of obstetrics will find the brief chapters at times both inadequate and over-dogmatic.

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## PRIZE OF THE INTERNATION FOUNDATION OF GYNAECOLOGY AND OBSTETRICS

THIS Prize worth 10,000 Belgian francs is awarded every four years. The next award will be on 1st July, 1958.

The work submitted may be in manuscript or published form. In the latter case only work published during the four years preceding the date of the award will be considered. Work which has received a previous award is not eligible.

Two copies of the work should be sent to The Secretariat of The Royal Belgian Society of Gynaecology and Obstetrics (Dr. R. Vokaer, 309 Avenue Molière, Brussels) before 1st July, 1957.

# REVIEW OF CURRENT LITERATURE

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## ANATOMY

59. **The Clinical Determination of Pelvic Outlet Capacity. An Adjunct to Roentgenometric Survey of the Upper Pelvis.**

By H. THOMAS and I. FRIEDMAN. *Amer. J. Obstet. Gynec.*, **72**, 635–640. Sept. 1956. 7 figs. 8 refs.

When abnormal narrowing of the pubic arch is present to a degree that denies to the head the anterior part of the arch the antero-posterior diameter is no longer a true index of outlet capacity. A truer index is the corrected or available antero-posterior diameter; that is the distance from a hypothetical pubic arch to the posterior end point, usually the tip of the sacrum. The authors use a metal ring gauge of 8·5 cm. diameter, adapted from the smaller 8 cm. solid gauge introduced by W. I. C. Morris in 1947. It is slipped under the arch as close to the symphysis as possible. If there is more than 1 cm. distance between the gauge and the symphysis the available antero-posterior diameter is determined by the internal hand or by callipers. The ring is steadied in position and the anterior tip of the callipers is brought to the top of the circle. The available antero-posterior diameter is the best index of outlet capacity, but if the arches are much narrowed the interspinous transverse diameter should be measured roentgenologically.

Outlet contraction may show itself as (1) abnormal shortening of the antero-posterior diameter as a part of a general funnel tendency in which transverse shortening of the interspinous distance is also present. (2) Transversely alone, by too prominent ischial spines. (3) Antero-posteriorly alone, by unusual convergence forward of the lower sacrum. (4) Narrowing of the pubic arch alone. The dictum of Morris is probably the final word in consideration of the antero-posterior diameter as the best index of outlet capacity. He stated that if the antero-posterior diameter of the plane of least pelvic dimensions measures at least 11·5 cm. serious antero-posterior narrowing of the outlet can be ruled out, since in the narrowest pelvic arches the corrected (available) antero-posterior diameter very seldom differs more than 1·5 cm. from the antero-posterior diameter of the inferior pelvic strait.

*F. J. Browne*

60. **The Cornual Sphincter of the Uterus.**

By R. G. HUNTER, G. W. HENRY and W. H. CIVIN. *Surg. Gynec. Obstet.*, **103**, 475–480. Oct. 1956. 9 figs. 14 refs.

This is the report on an investigation initiated in Honolulu, Hawaii, to determine whether a sphincter action exists at the cornual extremity of the endometrial cavity, and if it can be visibly demonstrated.

The films from 284 hysterosalpingograms were examined and in 80 per cent definite cornual constrictions of sphincter-like appearance were visualized on one or both sides. These constrictions are well illustrated in a number of reproductions of films from the series.

During salpingography, it was noted that discomfort occurred when the radio-opaque material reached the interstitial portion of the tube if the examination was performed during the proliferative phase of the menstrual cycle or pre-menstrually. When done at ovulation, the procedure produced practically no discomfort. This suggested changes in the cornual sphincter mechanism at different phases of the cycle. To investigate this, salpingography was performed on 5 normal parous women in the post-menstrual, ovulatory and pre-menstrual phases in the same cycle. The findings were quite uniform. High pressure was needed to fill the Fallopian tubes in the pre-menstrual and post-menstrual phases, whereas at ovulation the media practically flowed through the tract and spilled with no hindrance or discomfort.

The anatomical investigation of the cornual sphincter was done on uteri removed surgically for various reasons. It was noted that the tubal muscle is generally thin, and a narrow but well-defined bundle of fibrous tissue is interposed between this and the uterine musculature at the cornual orifice of the tube. The uterine muscle adjacent to the orifice is thick and often bulges into the uterine lumen when relaxed. This muscle is collected into a sphincter-like mass of interlacing bundles which completely circumscribes the tubo-uterine lumen. It is so situated that, by shortening and thickening of its individual fibres during contraction, it interrupts patency by bulging into and obliterating the lumen.

The authors conclude that interruption of tubo-ovarian continuity is due to the sphincteric action of this mass of uterine muscle and not to the relatively thin tubal muscle.

*John P. Erskine*

## PREGNANCY

**61. Hormones in Human Reproduction. Part I: Metabolism of Progesterone.**

By M. E. Davis, E. J. Plotz, G. V. LeRoy, R. G. Gould and H. Werbin. *Amer. J. Obstet. Gynec.*, **72**, 740–753. Oct. 1956. 6 tables. 9 figs. 57 refs.

By oral administration of labelled cholesterol to pregnant women it has been shown that cholesterol can serve as a precursor of steroid hormones including androsterone and pregnanediol, and that acetate, a precursor of cholesterol, can be converted into progesterone the synthesis ceasing after pregnancy is terminated. If labelled progesterone is administered intramuscularly in early pregnancy, appreciable quantities are found in the urine thus demonstrating the *in vivo* conversion of progesterone to pregnanolone and pregnanediol. Hence the pathway acetate–cholesterol–progesterone–pregnanolone–pregnanediol represents one of the principal physiological routes of synthesis and metabolism of progesterone in human pregnancy. This conclusion is supported by the results of perfusion of beef adrenals with tagged cholesterol, labelled progesterone being recovered in the perfusate, and by the recovery of labelled progesterone from the foetal side of the human placenta after perfusion with $^{14}C$ cholesterol.

It has recently been claimed that progesterone may be a precursor of adrenocortical hormones. If this is so, progesterone secreted by the placenta may serve as an additional precursor of adrenocortical hormones in human pregnancy. Having established the importance of acetate and cholesterol as hormone precursors the authors investigated the rate of synthesis of cholesterol in maternal and foetal endocrine glands during various phases of pregnancy. They found that after intravenous injection of acetate 167 minutes before therapeutic abortion at the 7th week of pregnancy the highest concentration of cholesterol was in the corpus luteum, and the concentration was equally high during the 12th, 17th, 18th and 19th weeks, thus refuting the usual view that the corpus luteum begins to regress at the 10th week.

Dietary cholesterol was quickly absorbed by the corpus luteum and placenta but there was very little in the foetal organs, indicating that only small amounts cross the placenta in early pregnancy though much more passed in the later weeks. These data indicate that an extremely fast local synthesis and a ready absorption of plasma cholesterol take place in the corpus luteum of pregnancy and in the foetal part of the placenta, and support the impression that a substantial part of progesterone may be derived from plasma cholesterol.

The present study shows that the foetus can synthesize cholesterol in its liver and adrenals, that it does not depend on maternal cholesterol transferred through the placenta and strongly favours the assumption that the foetal adrenals can produce hormones.

*F. J. Browne*

**62. Management of the Elderly Primigravida.**

By R. R. Fliehr. *Obstet. Gynec.*, **8**, 494–499. Oct. 1956. 9 tables. 5 refs.

The case histories of 309 primigravidae aged 35 and over were reviewed by the author from deliveries at Abbott Hospital, Minneapolis, Minnesota between 1935 and 1955. Labours were found to be longer than normal with an increased incidence of occipito-posterior positions, a higher incidence of toxaemias, and an increased stillbirth rate. The incidence of prolonged labour in patients over 40 was markedly increased, as was the stillbirth rate in this group.

When complications such as prolonged labour, toxaemia, foetal distress and the like are encountered, Caesarean section should be freely employed, for statistics indicate that only in this way can the high stillbirth rate in this type of case be reduced.

*J. G. Dumoulin*

**63. The Fertile Period as Indicated by 157 Conceptions Following Therapeutic Insemination.**

By E. J. Farris. *Ann. Ostet. Ginec.*, **78**, 16–20. 1956. 1 table. 1 fig. 5 refs. [In English.]

The duration of the fertile period in the menstrual cycle was studied in 157 conceptions following artificial insemination in 125 women.

The time of ovulation was determined by the "rat hyperaemia test". Early morning urine is injected into

immature rats which are killed two hours later by carbon monoxide gas. The presence of hyperaemia in the ovary indicates ovulation. Insemination was performed between the 10th and the 20th day of cycles varying from 20 to 38 days in average length. Computation of the average length of 3 consecutive cycles has been found to give the cumulative average for 12 cycles.

The largest number of conceptions occurred when insemination was practised one day before the mid-cycle date. Of all conceptions, 78·5 per cent occurred between days 11 and 14, and 25·5 per cent on day 12. The fertile period has been found to extend from 2 days before ovulation to 5 days after ovulation.

*Josephine Barnes*

**64. Estimation of Changes in Body Composition in Normal Pregnancy by Measurement of Body Water.**

By J. Seitchik and C. Alper. *Amer. J. Obstet. Gynec.*, **71**, 1165–1175. June 1956. 2 tables. 10 figs. 12 refs.

The purpose of this paper is the presentation of a working hypothesis for the significance of the accumulation of water in normal pregnancy. In normal non-pregnant individuals the total body water is a reflection of the size of the lean body mass, and these two bear a fairly constant relationship to each other, presumably because the water content of lean tissue is usually constant. On the other hand when we express the total body water as a percentage of the body weight we are providing an estimate of relative obesity. The study of body water therefore, provides an opportunity to estimate the size of the components of the body mass, and thus changes in weight may be identified as change in either the lean or the fat, or both.

Studies of nitrogen balance and total circulating protein suggested that pregnancy is characterized by gain in lean body mass far exceeding that accounted for by the conceptus and the maternal reproductive organs and blood volume. Indeed, these estimated gains exceeded the normal weight gain of the average gravida, and it was thought that an explanation might be that in pregnancy there was some loss of body fat.

To gain evidence on this point, total and extracellular water determinations were made on 7 pregnant women on several occasions throughout pregnancy, and 6 weeks post-partum. The body compositions were then computed by the formulae of McCance and Widdowson. The result was that the total body water increased throughout pregnancy, and in each pregnancy the total body water gained was greater than the weight gained. The bulk of the total body mass gained was equally divided between the second and third trimesters. The extracellular fluid increased during each pregnancy and the gain in extracellular fluid was proportionate to the gain in total body water.

Inasmuch as the gain in total water in pregnancy is greater than the weight increment, a considerable quantity of solid must have been lost. But only three significant masses of body solids exist; intracellular protein, bone mineral, and body fat. In normal pregnancy the nitrogen and calcium balance is positive, suggesting accumulation of protein and bone minerals. If nitrogen, water, and calcium are accumulated in a quantity exceeding the gain in weight the only possible interpretation is that lean body tissue is added and fat is lost. Reasons are given for believing that this loss is due to utilization of stored fat for lean tissue synthesis during pregnancy. If this is so, the nutritional state of the mother before pregnancy will determine her tolerance to calorie or nutritional deficiency. If the woman is normally proportioned for her height, mild deficiencies of protein or calories could be rectified from her own tissues, but if the fat stores are limited and the woman is protein deficient, this buffer is not available.

The authors believe that the changes in size of the various body water compartments are merely reflections of these changes in body composition. They found no evidence of selective accumulation of any of the body water compartments in normal pregnancy.

*F. J. Browne*

**65. Catheterization Studies of Cardiac Hemodynamics in Normal Pregnant Women with Reference to Left Ventricular Work.**

By D. J. Rose, M. E. Bader, R. A. Bader and E. Braunwald. *Amer. J. Obstet. Gynec.*, **72**, 233–246. Aug. 1956. 4 tables. 6 figs. 36 refs.

This work was done on 46 normal pregnant women. Each patient was studied once during gestation from the 14th week to one day before term; observations were made both at rest and during exercise. The results confirm those got in 88 normal pregnant women by Palmer and Walker (*J. Obstet. Gynaec. Brit. Emp.*, 1949, **56**, 537) using a similar technique at the Post-Graduate Medical School, London, and by Hilary Hamilton, Edinburgh (*J. Obstet. Gynaec. Brit. Emp.*, 1949, **56**, 548) in 92 women, 68 of whom were pregnant.

The present authors found that there was an increase in cardiac output at rest at the earliest period of gestation studied (14th week), reaching a maximum of 40 per cent greater than that in non-pregnant controls at the 25th to the 27th weeks of pregnancy then falling progressively to normal just before term. This was accomplished by a reciprocal change in arteriovenous oxygen difference while oxygen consumption was only slightly increased. A redistribution of blood late in pregnancy with a decrease in the intrathoracic blood volume and pooling of blood in the lower extremities may explain the fall in cardiac output in the presence of increased plasma volume. There was no indication of any impairment of myocardial reserve.

*F. J. Browne*

**66. Some Haematological Aspects of Pregnancy.**

By L. Whitby. *N.Z. med. J.*, **55**, 355–360. Oct. 1956.

This paper provides a valuable summary of the physiological changes that take place in the blood in pregnancy, and the common blood disorders that are observed in pregnancy.

Anaemia is one of the prime haematological aspects of pregnancy, and all anaemias due to pregnancy *per se* are nutritional from lack of some essential haemopoietic factor. Certain clinical rules are presented. Because of

the foetal demands on iron, and the iron deficiency that may follow blood loss at delivery, the administration of small doses of iron in a palatable form is prudent. Ferrous gluconate is best tolerated. Megaloblastic anaemia is also a deficiency syndrome which remits when the pregnancy terminates. Folic acid, potentiated with ascorbic acid is usually curative. Untreated cases have a high mortality.

Less common problems are leukaemia, Hodgkin's disease and polycythaemia. Pregnancy has apparently no effect on the progress of these diseases so termination of the pregnancy is not indicated. Irradiation as a method of treatment for the mother is undesirable, unless there is adequate shielding of the foetus. In the author's experience there is no familial transmission of leukaemia.

Acute and chronic forms of thrombocytopenic purpura occur in pregnancy. In principle, these conditions do not warrant termination of pregnancy, since treatment usually controls the disease. Fresh blood transfusions are usually effective, and splenectomy may be performed after term, or even during pregnancy if the haemorrhagic state is severe.

Fibrinogen deficiency is next dealt with. A simple bedside test of observing the clotting of a small quantity of blood should be followed by a quick chemical method of estimating the fibrinogen content. The critical level is 200 mg., and the use of fibrinogen, dried plasma, or several litres of blood is advised to restore the fibrinogen to this level.

Immunization phenomena are finally discussed, and the principles of investigation and treatment of Rhesus-incompatibility are given.

*L. Woodrow Cox*

67. **Continuous Integration of the Foetal Heart Rate.** By D. H. SMITH and H. M. CAREY. *N.Z. med. J.*, **55**, 309–312. Aug. 1956. 6 figs. 13 refs.

A miniature crystal microphone is mounted in a shell of sponge rubber and metal, and strapped to the patient's abdomen over the site of maximum audibility of the foetal heart. It is rather heavy for the patient's comfort, but records foetal heart sounds without extraneous noise. This is connected to an amplifier accentuating sounds in the frequency range 60–80 c/s. and is (comparatively) insensitive to sounds outside this range. This is connected to a pulse rate counter, to cover the range 75 to 190 per minute. The counter includes a "gate" which remains closed, keeping the circuit insensitive for a pre-set time after the reception of a pulse; thus it ensures that after registering the first heart sound, the counter cannot operate again until the second heart sound has finished.

Good results are obtained, except that alterations in the patient's position during labour may interfere with the record. The apparatus records graphically, the foetal heart rate being plotted against time. Illustrations of the apparatus and the recordings are given.

*L. Woodrow Cox*

68. **A Study of the Foetal Circulation in the Placenta by Injection of Synthetic Resins.** (A propos de l'étude de la circulation foetale dans le placenta par l'injection de résines synthétiques.)

By J. THOYER-ROZAT and —. MARTIN. *Gynéc. Obstét.*, **55**, 255–256. 1956. 4 figs. 1 col. plate.

To study the placental circulation the authors cut the cord 10 cm. from its insertion after washing both surfaces of the placenta. Both the umbilical vein and the two umbilical arteries were carefully dissected up for 1 cm. Needles were introduced into each of the three vessels and stitched in position using a nylon thread. Injection was carried out using a pigmented solution of vinyl resin diluted to 20 per cent strength with acetone. The fluid was slowly and continuously injected in such a way that the greater part of the cotyledon capillaries were filled. The placenta was then placed in cold water for 24 hours and then immersed in fuming hydrochloric acid for forty-eight hours. It was finally washed in water.

The authors found that the intra-cotyledonary plexus comprises for each cotyledon a well-developed villous trunk which is separate from the umbilical vessels or their ramifications. This trunk, which is ½ to 1 cm. in diameter, is buried in the chorion, the artery showing a spiral series of turns around the vein. These vessels of the first category of large calibre give off smaller branches of the second category which run horizontally, and from these arise at right angles even smaller branches of the third category. Sometimes these are rectilinear and sometimes arch shaped.

There are four excellent colour photographs.

*D. Maxwell*

69. **A Report on the Distribution and Character of the Vessels and Foetal Capillaries in the Human Placenta.** (Observations sur l'aspect et la disposition des vaisseaux et capillaires foetaux dans le placenta humain.)

By M. MAYER, M. PANIGEL and H. LECLERC-POLYAK. *Gynéc. Obstét.*, **55**, 257–280. 1956. 13 figs. 1 col. plate. 37 refs.

The authors' material consisted of over 200 placentae, of which 120 were submitted to lavage-perfusion and injections. The majority of specimens were obtained after spontaneous delivery at term, but the writers also dealt with 12 placentae obtained at Caesarean section and numerous others expelled in good condition in the course of miscarriages at different stages of pregnancy.

Lavage-perfusion injection technique consists of catheterization of the umbilical arteries after dissection of the vessels from Wharton's jelly a little above their anastomosis near the insertion of the cord. The liquid used was physiological serum to which was added an anticoagulant such as heparin or sodium citrate. The pressure used was never more than 120 cm. of water. The duration of the perfusion varied between 5–24 hours.

Various techniques were used:

(*A*) By corrosion: (*a*) Polymerization *in situ*. (*b*) Injection of derivatives of acetone.

(*B*) By intravascular injection of dyes and colloidal suspension. These included Chinese ink, Prussian blue, carmine, colloidal suspensions of heavy metals (such as gold and silver) made by Crookes, and were employed immediately after the specimens had been perfused with

physiological serum, using a pressure of less than 1 m. of water.

The writers discuss the different views of Bumm, Spanner and Stieve, and support the conception of Bumm as shown by the casts they have made, photographed and drawn.

*D. Maxwell*

**70. A Study of the Placental Circulation in Normal and Pathological Pregnancy.** (Étude de la vascularisation placentaire au cours des grossesses normales et pathologiques.)

By R. PALLIEZ, M. DELECOUR, A. FOVET and R. DEPREUX. *Gynéc. Obstét.*, **55**, 312–323. 1956. 11 figs.

The authors examined 100 placentae, some by ordinary anatomical study and others after injecting substances opaque to X-rays into the vessels.

In general the writers confirm the work of Wilkin (1954) but they disagree on 2 points: First, in central insertions of the cord, the arrangement of the arteries to the chorial plaque are not always symmetrical, and secondly, in eccentric insertions of the cord one of the two umbilical arteries may be absent (9 times out of 33).

The placental blood supply is described in 30 cases of normal pregnancy and in 20 cases of abnormal pregnancy where twins, infarction and postmaturity were concerned.

*D. Maxwell*

**71. Retinal Changes and Fetal Prognosis in the Toxemias of Pregnancy.**

By A. SADOWSKY, D. M. SERR and J. LANDAU. *Obstet. Gynec.*, **8**, 426–431. Oct. 1956. 2 tables. 3 figs. 10 refs.

From 1952 to 1955 there were 176 births complicated by toxaemia of pregnancy (2·2 per cent) among 7,976 births at the University Hospital, Jerusalem. One hundred and one of the toxaemic cases were mild, 51 severe and 15 were of renal disease. The fate of the foetus in toxaemic cases may be difficult to predict; for example, the maternal condition may border on eclampsia and yet the foetus be born alive, while in another instance when the toxaemia improves with treatment the foetus may die.

The authors show that the severity of retinal vascular changes is allied to the foetal mortality rate. An assessment of foetal prognosis may be obtained by a combination of the degree of severity of the toxaemia and the degree of retinal change. In mild and severe cases of toxaemia there was no foetal death in the series where there was no change in the retina. Pregnancy should be terminated prematurely in cases of severe toxaemia with Grade 2 or more fundal changes.

*J. G. Dumoulin*

**72. Measurement of Aldosterone in the Eclamptogenic Toxemias of Pregnancy.**

By A. C. BARNES and E. J. QUILLIGAN. *Amer. J. Obstet. Gynec.*, **71**, 670–682. Mar. 1956. 6 figs. 30 refs.

The authors made quantitative determinations of the Sodium Retaining Fraction (S.R.F.) in 12 normal pregnant women and in 34 toxaemic patients. Five of the latter had only an increased blood pressure (average 130/90), with excessive weight gain, with some albuminuria in 2 cases. Of the remaining 29, 4 had eclampsia, 12 had severe and 13 mild pre-eclampsia.

The group with toxaemia showed a marked increase in S.R.F. compared with the normal pregnant women. Many of the non-toxaemic group, however, showed as much S.R.F. as the mean for the toxaemic group, while several of the toxaemic patients overlapped well into the normal range. There was, too, a negative correlation with the severity of the toxaemia, the patients with mild toxaemia showing more S.R.F. than those with eclampsia. There was no evidence of the presence of any sodium retaining fraction in 5 placentae from toxaemic women.

Attempts to increase the S.R.F. by giving progesterone, oestrogens or cortisone were not successful, but evidence was got that ACTH might increase the aldosterone.

*F. J. Browne*

**73. Eclampsia in New Zealand, 1954-55. Report of the Obstetrical Research Sub-Committee of the Medical Research Council (N.Z.).**

*N.Z. J. Med.*, **55**, 220–222. June 1956. 2 tables.

In 1954 among 55,112 births there were 67 cases of eclampsia (1·21 per 1,000), and in 1955 among 56,564 births there were 58 cases (1·02 per 1,000). In the two years there were 3 maternal deaths and 22 infant deaths. In the 14 fatal cases in the six years 1950–55, the causes of death were cerebral haemorrhage (5), sudden cardiac failure (5), and anuria (4). There was not a single case in which convulsions persisted uncontrolled, leading to gradual exhaustion with coma and pulmonary oedema. Caesarean section was performed 10 times (1 maternal death) in the 2 years.

*L. Woodrow Cox*

**74. Etiology of Pre-eclampsia–Eclampsia. VI. Sodium, Potassium, Nitrogen, and Water Content of Muscle and Skin in Pre-eclampsia.**

By W. J. DIECKMANN and R. E. POTTINGER. *Amer. J. Obstet. Gynec.*, **71**, 596–613. Mar. 1956. 5 tables. 5 figs. 14 refs.

Several reports based on small numbers of cases, mostly autopsy material, state that in eclampsia there is an enormous increase in muscle sodium. In the present investigation pieces of rectus muscle and abdominal skin were taken at Caesarean section from patients with pre-eclampsia, eclampsia, hypertensive disease, and normal pregnancy, and from non-pregnant women at gynaecological operations, and analyzed for sodium, potassium, nitrogen, and water, after removal of fat and blood.

Contrary to expectation and previous observations it was found that the water content of muscle and skin in pre-eclampsia and hypertensive disease was unchanged as compared with normal pregnancy, but that the sodium ion concentration was significantly decreased, and was indeed the same as in the non-pregnant woman. Potassium concentration was unchanged. These findings are at present inexplicable.

Nitrogen content of muscle was the same in non-pregnant and normal pregnant women, in pre-eclampsia and in hypertensive disease.

*F. J. Browne*

**75. Clinical Trial of Buclizine Hydrochloride for Vomiting of Pregnancy.**

By M. P. DURHAM. *Brit. med. J.*, **2**, 1276–1277. Dec. 1, 1956. 3 tables. 2 figs. 4 refs.

The author, from the Royal Victoria Hospital, Folkestone, treated 33 patients complaining of vomiting of pregnancy with buclizine hydrochloride ("vibazine"). It is an antihistamine of low toxicity. The majority of cases were of mild degree, and in the first 14 weeks of pregnancy.

A dose of 50 mg. at night and 25 mg. in the morning was found most satisfactory. Complete relief was described in 53 per cent of patients and improvement in 14 per cent. Many patients were relieved in 48 hours. The only adverse effects were drowsiness if large doses were given in the daytime. Only 3 patients complained of deterioration.

*Eileen Wilson*

**76. The Treatment of Incomplete Abortion.**

By J. E. DAVIS. *West. J. Surg. Obstet. Gynec.*, **64**, 588–591. Nov. 1956. 11 refs.

The author defines this condition as remnants of the products of conception, before viability, remaining within the uterine cavity complicated or not by infection and/or haemorrhage. Treatment consists of either early curettage or conservative methods, and the literature is reviewed. Infection is either invasive or non-invasive, the latter being limited to the mucosa and produced by saprophytic bacteria. The organism of invasive infection is commonly an anaerobic streptococcus and is ordinarily non-pathogenic, only becoming virulent in the presence of traumatized or devitalized tissue, a fact that should urge gentleness in operative manipulation. Infection with Group A β-haemolytic streptococci is an absolute contra-indication to curettage. The author advocates a compromise between early curettage and frank conservatism. Particular attention is paid to the history and examination of the patient to ensure that the diagnosis is correct. A speculum is passed and debris removed from the cervical canal, a swab being passed into the uterine cavity and a culture prepared. Sedatives are given to alleviate pain and pituitrin ·05 ml. given every 30 minutes for 6 doses; if examination then shows that the uterus is empty, ergotrate is given 4-hourly for 6 doses. If the uterus is not emptied and bleeding is minimal one may wait, but if the bleeding becomes profuse, re-evaluation should take place and, in most cases, curettage should be performed. Pituitrin is given intra-muscularly beforehand and the bulk of the tissue removed with sponge forceps and blunt curette. All tissue should be removed, if necessary with a sharp curette, and there should be no further bleeding. Packing is almost always unnecessary. Attention should be given to the possibility of uterine malformation being the cause of the abortion. The culture should be read in 18–24 hours; if there are no Group A β-haemolytic streptococci present and the abortion is incomplete, curettage should be performed. Early ambulation and discharge from hospital should follow. In the presence of haemolytic streptococci curettage should not be performed until the infection is controlled by antibiotics unless there is profuse haemorrhage.

[The dose of pituitrin is given in the paper as ·05 ml. although this seems very small.]

*D. C. A. Bevis*

**77. Gingival Tumors of Pregnancy. Review of "Pregnancy Tumors" and a Report of Two Cases.**

By F. J. ZARKA and M. M. STARK. *Obstet. Gynec.*, **8**, 597–600. Nov. 1956. 2 tables. 5 figs. 11 refs.

The authors present 2 cases of tumour of the gingivae occurring during pregnancy with a review of the literature. The gingival tumour of pregnancy usually occurs as a single lesion with a predilection for the upper incisor region. It is purplish in colour with a red border and may ulcerate. It seldom exceeds 2 cm. in size, occurring usually between the third and fifth month of pregnancy. It persists post-partum and enlarges in the next pregnancy. The histological picture shows a mass covered by squamous epithelium with a stroma similar to that of a fibroangioma. Surgical excision is the best treatment.

*J. G. Dumoulin*

**78. Pregnancy and Lupus Erythematosus.**

By E. A. FRIEDMAN and J. W. RUTHERFORD. *Obstet. Gynec.*, **8**, 601–610. Nov. 1956. 7 tables. 4 figs. 39 refs.

Lupus erythematosus may present itself with diverse manifestations. It is usually a chronic disorder with a remittent course, but it may also be a fulminating rapidly fatal condition. The aetiology is unknown, and it is at present classified among the collagen disorders. Therapy has been almost entirely non-specific. The introduction of cortisone and adrenocorticotropic hormone has led to increasing numbers of early remissions associated with dramatic amelioration of constitutional symptoms.

The authors review 188 female patients with lupus erythematosus from the Presbyterian Hospital, New York City, between 1932 and 1955. Of these, 117 had been married and 101 had the disease during the reproductive era. Eighty of the cases had 181 pregnancies between them, suggesting that the disease does not affect fertility.

In 29 patients the disease was intimately linked with one or more pregnancies (42 in all). There was an excessive number of premature births (15·8 per cent) and spontaneous abortions (23·7 per cent) particularly in the acute and subacute disseminated cases. If, however, the pregnancy is carried to viability the infant is apparently unaffected by the maternal disease.

The effect of pregnancy upon the course of the disease is as follows. Most patients with the acute and subacute disseminated form experience subjective relief. The basic disease process, however, is not apparently affected by the pregnancy; both exacerbations and remissions are found in nearly equal numbers in early pregnancy.

The disease resumes its pre-pregnancy status post-partum, usually within 2 months. Exacerbations are the rule, since so many become clinically quiescent during the pregnancy.

It seems that no real beneficial effect on the course of the disease results from therapeutic abortion.

*J. G. Dumoulin*

79. **Pregnancy and Cretinism. Report of a Case and Review of the Literature.**

By A. M. SIEGLER. *Obstet. Gynec.*, **8** 639–641. Nov. 1956. 1 table. 13 refs.

The case reported by the author was diagnosed as a cretin at the age of 1 year. She was placed on 3 g. of desiccated thyroid daily which she presumably had been taking since 1923. She had a bloated face and puerile expression. The voice was high pitched and squeaky, and her speech was slow and often inarticulate. In 1955, a Caesarean section was performed on her for breech presentation and acute toxaemia, a healthy baby being born.

The incidence of pregnancy in the cretin is very low, the author having found only 8 other reported cases in the world literature.

*J. G. Dumoulin*

80. **Congenital Polycystic Kidney Disease in Pregnancy.**

By R. LANDESMAN and L. SCHERR. *Obstet. Gynec.*, **8**, 673–680. Dec. 1956. 2 figs. 16 refs.

The adult type of polycystic kidney disease is rare and usually is recognized at about the time of the menopause. Consequently, the disease is asymptomatic during childbearing years. Twenty-eight women who had 64 pregnancies and polycystic disease are reported from the New York Hospital—Cornell University Medical College, New York. Of these, only 5 had known disease during pregnancy.

Diagnosis is usually made by pyelography when bilateral enlarged kidneys may be seen. Heredity is an important aetiological factor. Because, in the majority of cases, clinical manifestations of the renal condition do not appear until around the time of the menopause, most of the pregnant women who later develop such manifestations have normal pregnancies and deliveries. Twenty-three of the 28 cases fell into this category: there was no evidence that pregnancy hastened the development of the disease. The remaining 5 women all had an elevated blood pressure but only 1 had renal insufficiency. A raised blood pressure alone does not contra-indicate pregnancy, and in such cases the authors have found reserpine a useful drug.

*J. G. Dumoulin*

81. **Pregnancy Complicated by Amyotrophic Lateral Sclerosis.**

By J. W. HUSTON, J. LINGENFELDER, D. W. MULDER and L. T. KURLAND. *Amer. J. Obstet. Gynec.*, **72**, 93–99. July 1956. 1 table. 7 refs.

This disease is relatively common in the island of Guam and the authors report on 17 patients who had a total of 21 infants. Apart from the supervention of pregnancy, it is always fatal in from 3 to 4 years. Pregnancy did not seem to influence its course, nor did the disease seem to have any effect on the pregnancy, though the enlarged uterus might add to already existing respiratory difficulties. The most serious complications were secondary to the paralysis of the facial, oral and laryngeal muscles with consequent inability to take adequate nourishment. For some patients nasal feeding or gastrotomy may become necessary. As the smooth muscle of the uterus is not affected labour was normal in all cases and the child was not affected by the disease. In most cases the mother will not be able to care for her child through its infancy and it is almost certain that she will be dead before it is 3 years old.

*F. J. Browne*

82. **Subarachnoid Hemorrhage and Pregnancy.**

By D. E. CANNELL and E. H. BOTTERELL. *Amer. J. Obstet. Gynec.*, **72**, 844–852. Oct. 1956. 8 tables. 31 refs.

This is a report on 16 cases of subarachnoid haemorrhage occurring in pregnant women. Of these, 2 were associated with pre-eclamptic toxaemia, 1 each with thrombosis of the superior sagittal sinus, and mycotic aneurysm following subacute bacterial endocarditis, 6 with intra-cranial aneurysm, 3 with arteriovenous malformations, and in 3 the cause was not determined.

As to diagnosis severe (often occipital) headache, nuchal rigidity, nausea and vomiting, loss of consciousness, hemiplegia and involvement of cranial nerves were present in that order of frequency. The diagnosis was confirmed by withdrawal of gross bloody spinal fluid under pressure and cerebral angiography.

Treatment is the same as in the non-pregnant. Neurosurgical operations have lowered the mortality considerably and should be done as soon as possible after the initial haemorrhage. Contra-indications are coma, extreme neurological damage and the presence of multiple anomalies of the cerebral circulation. Of the 16 cases, 5 died.

*F. J. Browne*

83. **A Review of 463 Early Ectopic Pregnancies Operated Upon at the Groote Schuur Hospital.**

By H. F. MUKHEIBER. *S. Afr. med. J.*, **30**, 1165–1167. Dec. 1, 1956. 3 tables. 3 figs. 3 refs.

The author has reviewed 463 cases of ectopic pregnancy admitted to the Groote Schuur Hospital, Cape Town, in the 5-year period 1951–1955. As there were 12,682 admissions, the incidence was 3·6 per cent. The majority of cases were in the 25 to 40 year age group. Fifty-eight per cent belonged to the Coloured race. The numbers of Bantu and White patients were the same (21 per cent). Tubal inflammatory disease is probably the greatest single cause. A history of pelvic infection was elicited in 27 per cent of cases, but histological confirmation was obtained only in 13 per cent. Three cases were of tuberculous origin. The diagnosis of pelvic infection has decreased from 62 per cent in 1946 to 24 per cent in 1955 at the gynaecological out-patient department. This is no doubt due to the antibiotics. Considering the number of ectopic pregnancies, the number of admissions and the population increase, it seems that the increased number of tubal pregnancies has kept in trend with the rise in both the population and the number of admissions. The main symptoms were abdominal pain (95 per cent),

shoulder and subcostal pain (28 per cent), amenorrhoea (82 per cent), vaginal bleeding (74 per cent), gastro-intestinal symptoms (42 per cent), and bladder symptoms (18 per cent). The gastro-intestinal symptoms were nausea, vomiting and diarrhoea. Three cases presented with retention of urine.

Accurate pre-operative diagnosis was made in 65 per cent of cases. The wrong diagnoses were tubo-ovarian masses (17·4 per cent), fibroids (4·2 per cent), abortions (4 per cent), ovarian cysts (3·7 per cent), appendicitis (2·1 per cent) and others (3·6 per cent). In 22 cases laparotomy was performed following an erroneous diagnosis. A falling haemoglobin reading was found to be a valuable diagnostic guide. Frog tests were of minimal help. Colpopuncture prolongs the anaesthetic and may produce false positive and false negative results. It was used as an aid in 72 cases. In this series there were 2 deaths. This was a mortality of 0·4 per cent. One patient died shortly after admission, and the other succumbed on the 7th post-operative day as the result of a massive pulmonary embolus.

At Groote Schuur Hospital operation is undertaken as soon as the diagnosis is made. Blood transfusion was given in 82 per cent of cases. The following operations were performed: right salpingectomy (187 cases), left salpingectomy (176 cases), salpingo-oöphorectomy (87 cases), wedge resection of the uterus (11 cases) and oöphorectomy (1 case).

Total salpingectomy is advocated as the risk of recurrence is high. In this series it occurred in 6·3 per cent of cases. Conservation should be reserved for cases in which the other tube has already been removed. The author does not favour oöphorectomy as suggested by Jeffcoate, as there are no known figures to substantiate his statement. Wedge resection and not hysterectomy should be performed for interstitial pregnancy. The opposite adnexa should always be inspected. Post-operative complications were few. Sixteen patients had complications involving the lungs. The majority were probably cases of pulmonary embolus.

*Author's Abstract*

**84. Ruptured Tubal Pregnancy. Aids in Diagnosis and Treatment.**

By B. WORD. *Obstet. Gynec.*, **8**, 627–635. Nov. 1956. 6 tables. 1 fig. 10 refs.

Ruptured tubal pregnancy occurs about 20,000 times annually in the United States. In the last 10 years, there were 2,277 deaths from ectopic gestation, a rate of 6·3 per 100,000 live births. During those 10 years (1945–1954) there were 382 ectopic pregnancies at University and St. Vincent's Hospital, Birmingham, Alabama, with 3 deaths.

Of the 382 cases, 379 had abdominal pain, 329 had vaginal bleeding and 264 had amenorrhoea. Signs include abdominal tenderness either over the lesion or more generalized. Rigidity is not present unless the patient is seen soon after the initial rupture. If intra-abdominal haemorrhage has continued for some time, the abdomen becomes distended and doughy. A ruptured ectopic gestation will cause exquisite tenderness on moving the cervix. In 183 patients a pelvic mass was recorded. Seventeen per cent were admitted in a state of shock. Many patients go into a temporary shock-like state initially. Aspiration of the pouch of Douglas was used in 201 cases of the above series, and non-clottable blood was obtained 192 times.

Treatment is always surgical. The author believes that in the very shocked case, blood transfusion should be given before and during the operation rather than during and after it. Total excision of the affected tube is recommended.

*J. G. Dumoulin*

## LABOUR

**85. Some Public Health Aspects of an Outbreak of a Penicillin-Resistant Staphylococcal Infection in a Maternity Hospital.**

By A. DOUGLAS and H. T. KNIGHTS. *N.Z. med. J.*, **55**, 378–387. Oct. 1956. 2 figs. 18 refs.

On 22nd November, 1955, the District Office of the Health Department was notified by the matron of a maternity unit of a private hospital that five babies had died of a (staphylococcal) infection affecting their respiratory tract. One baby had died within the maternity unit, the others had died in the public hospital, to which they were admitted either directly from the maternity unit, or from their own homes after discharge from the unit. Other similar cases were being nursed in the maternity unit in isolation. The maternity unit was closed pending investigation. Three more babies died, bringing the total to eight. The post-mortem findings were similar, staphylococcal pneumonia, lung abscess and empyema in various combinations.

A widespread swabbing programme was begun among the staff of the maternity unit, and nursing techniques were checked in all maternity units in the city. Obstetricians and other maternity unit staffs were asked for information about similar cases. As a result of the investigation 98 mothers were visited in their home. Of these, 13 had breast abscess, two had other skin lesions, and 39 babies had upper respiratory symptoms, 61 had skin lesions and 2 had eye lesions, Phage typing was undertaken, and in many cases a penicillin resistant staphylococcus phage type 80/81 was cultured from the lesions.

The details of the investigation, nursing technique and construction of the maternity unit are described. Recommendations for the control of infection are made. It is suggested that overcrowding was the prime factor in the outbreak. The particular maternity unit affected was one of the most popular in the city, with a minimum of confinements of 2·2 per bed per month and a maximum of 3·6 per bed per month in the period under review. Other maternity units in the city ranged between 1·6 and 2 per bed per month.

*L. Woodrow Cox*

**86. Labor in Multiparas. A Graphicostatistical Analysis.**

By E. A. FRIEDMAN. *Obstet. Gynec.*, **8**, 691–703. Dec. 1956. 2 tables. 11 figs. 43 refs.

This is a study of the rate of dilatation of the cervix in 500 multiparous labours. The graphs record the cervical dilatation plotted against a time abscissa, which gives a sigmoid curve, and the mean labour curve for the 500 cases was worked out. A study was made of those labours in which the curve differed from the normal in an attempt to demonstrate aetiological points. The effect of various factors on the pattern of the curve was studied, such as parity, sedation, pitocin, disproportion, occipito-posterior position, time of rupture of membranes, infant weight and maternal age.

*J. G. Dumoulin*

87. **Delivery of Elderly Primigravidas.**

By H. FREDRIKSON and A. ANBERG. *Acta obstet. gynec. scand.*, **35**, 483–494. 1956. 7 tables. 28 refs.

The authors, writing from the Department of Obstetrics and Gynaecology of Gothenburg (Sweden) University, present a comparison of a series of 433 primigravidae aged 35 years and over with a series of an equal number of primigravidae between 18 and 25 years of age. The elderly primigravidae constituted 2·8 per cent of the total number of obstetric admissions, and 6·3 per cent of all primigravidae.

There was no difference in the incidence of pre-eclamptic toxaemia in the 2 groups. Breech presentations were more common among the elderly women occurring in 6 per cent as compared with 3 per cent in the younger age group. Labour was of longer duration in the elderly primigravidae, 26 hours on the average against 16 hours in the younger women. The incidence of forceps delivery was 18 per cent in the elderly, but only 3 per cent in the younger women. Caesarean section was done in 14 per cent in the older group as compared with 1 per cent in all pregnancies.

The authors conclude that their perinatal foetal loss of 3·9 per cent in the elderly primigravidae could have been reduced by more Caesarean sections.

*N. Alders*

88. **The Cape Town Obstetric Flying Squad: Its Inception, Organisation and Operation.**

By C. J. HAGBERG. *S. Afr. med. J.*, **30**, 1140–1144. Nov. 24, 1956. 3 tables. 2 figs. 1 ref.

If all deliveries could be conducted in hospital, an obstetrical emergency service would not be necessary. The author discusses the history of the "flying squad", commencing with the work of Joseph DeLee in Chicago at the end of the last century. In the U.K. it was initiated by Farquhar Murray.

The Cape Peninsula is a unique testing ground for such a service. The obstetrical beds are as yet inadequate for the large population, many of whom are unaware of the advantages of antenatal and intra-partum care. The unit commenced operating in September, 1953, and a period of 33 months is reviewed. The equipment is listed. Three separate and complete sets are always in readiness at the Peninsula Maternity Hospital. The squad may be summoned by any doctor or midwife in the Peninsula. The team is made up of an obstetrical registrar and house-surgeon, a trained sister or staff-nurse and a pupil midwife, and 2 medical students undergoing resident training in the hospital.

The operation of the unit is discussed. Usually it has left the hospital within 15 minutes of the call being received. The total number of calls in the period reviewed was 192. This has increased from an average of 3–4 a month to an average of 8 a month. The author describes the areas visited and the conditions encountered. In a few cases it was necessary to carry the equipment over a mile as the ambulance could go no further. Of 165 patients treated for post-partum haemorrhage, the placenta was retained on arrival in 60 cases. In 2 patients bleeding had occurred before the birth of the second twin. There were 3 cases of secondary post-partum haemorrhage and 2 of traumatic haemorrhage. In this group manual removal was performed in the patient's home on 33 occasions. This was done when the blood pressure had reached 80 mm. Hg and an attempt at expression had failed. As the result of a few unpleasant anaesthetic experiences (as the patients had often had something to eat or drink), manual removal was performed with the aid of morphine ¼ gr. given intravenously. This method worked well and it is being further investigated. Other cases treated were ante-partum haemorrhage (14), abortions (3), retained placenta without post-partum haemorrhage (5), eclampsia (4) and 1 case of iron deficiency anaemia diagnosed post-partum. Cases of ante-partum haemorrhage were resuscitated and transported to hospital. The eclamptics were sedated with intravenous pentothal and magnesium sulphate followed by 50 per cent dextrose. They were then admitted to hospital.

The procedures carried out are listed and the maternal deaths reviewed. In 3 cases the patients were dead on arrival. The remaining 3 were moribund and died shortly after arrival of the squad. In 2 cases manual removal had been performed without resuscitation before the squad arrived. In all cases of post-partum haemorrhage the administration of ergometrine is advised while awaiting the arrival of the unit. Adequate facilities and delivery in hospital would certainly have prevented many of these deaths. No patients succumbed in the ambulance or in the hospital to which they were transported.

*Author's Abstract*

89. **The Uterine Omentum of the Rat and Its Response to Vasoconstrictor Drugs.**

By R. LANDESMAN and B. MENDELSOHN. *Amer. J. Obstet. Gynec.*, **72**, 84–92. July 1956. 2 tables. 4 figs. 23 refs.

The fatty omentum which lies on either side of, and is attached to, each uterine horn of the rat contains blood vessels that are a continuation of those supplying the uterine horns. This omentum was exteriorized over a transparent plastic chamber for direct microscopic observation and kept moist by a drip of warm Ringer solution. It was then used for testing the vasoconstrictive effect of the topical application of various drugs commonly used for induction of labour in severe pregnancy toxaemia.

It was found that the vasoconstrictor effect of commercial pitocin was 10 times that of purified or synthetic oxytocin. Purified vasopressin and pitressin also showed high vasoconstrictor activity. The authors concluded that pure and synthetic oxytocin may be less liable to cause foetal death from peripheral vasoconstriction than is commercial pitocin and are therefore preferable for clinical use.

*F. J. Browne*

**90. Clinical Evaluation of Relaxin.**

By C. E. Folsome, T. Harami, S. R. Lavietes and G. M. Massell. *Obstet. Gynec.*, **8**, 536–544. Nov. 1956. 5 tables. 18 refs.

The authors used relaxin in 58 pregnant women. Forty were in premature labour while the 18 others although at full-term by dates were thought to have small or premature babies. The dose of relaxin recommended was an initial 80 mg. (4 ml.) intramuscularly to be followed by 40 mg. at 4-hour intervals for 48 hours following cessation of all uterine contractions. The total dosage per patient varied from 80 mg. to 2,360 mg. Most premature labours were halted by the third injection. The drug should be reserved for those cases with "unfavourable" cervices—the type of case in which it is most likely to succeed. If used in such cases, it is effective in many instances in aiding foetal salvage in premature labour.

*J. G. Dumoulin*

**91. The Hormone Relaxin in Labor. Tocometric Studies of its Effect on Uterine Contractions at Term.**

By J. V. Kelly and N. Posse. *Obstet. Gynec.*, **8**, 531–535. Nov. 1956. 2 figs. 17 refs.

Recently there have been reports on the ability of relaxin-containing preparations to inhibit uterine contractions in premature labour. Using a new method of internal hysterography, the authors have obtained tocographic records from 25 women in early labour to whom relaxin was administered intravenously in varying doses.

In only one of the 25 patients did relaxin have a definite effect in reducing and inhibiting the uterine contractions of early labour.

*J. G. Dumoulin*

**92. Foetal Exsanguination Associated with Surgical Induction of Labour.**

By J. K. Russell, D. F. Smith and R. Yule. *Brit. med. J.*, **2**, 1414–1415. Dec. 15, 1956. 2 refs.

The authors describe two cases in which puncture of the membranes by the Drew-Smythe catheter caused death of the foetus from haemorrhage. In both cases the fluid withdrawn was heavily blood-stained and the foetus later succumbed. A puncture wound was found in each case on the foetal aspect of the placenta, with a tear in a foetal vessel. Both babies showed evidence of exsanguination.

The authors suggest that when a blood-stained tap is obtained with a Drew-Smythe catheter, the sample should be checked for the presence of foetal blood.

*Eileen Wilson*

**93. Shortness of the Umbilical Cord.** (De la brièveté du cordon.)

By A. J. Bret and F. J. Coupez. *Gynéc. Obstét.*, **55**, 240–249. 1956. 2 figs. 9 refs.

Five cases of dystocia associated with shortness of the cord collected in 5 months at the Creteil Maternity Hospital, Paris, led the writers to study this abnormality. They review the literature, including historical references.

The authors do not confirm the view that shortness of the cord is always associated with oligohydramnios; they found polyhydramnios in one case. They refer to Young's case of a mother who had two successive babies with cord lengths of 2·5 and 2·7 cm. True shortness of the cord is rarely associated with other congenital malformations. They found one case with umbilical hernia and deficiency of the abdominal wall in which the cord measured 15 cm.

As a rule diagnosis is impossible during pregnancy, but during questioning after delivery one of the authors' cases described a pain in pregnancy which they thought might have been diagnostic, and this was associated with small vaginal shows. During labour delay in labour, unexplained foetal distress, or vaginal bleeding may be noticed.

As regards treatment the authors recommend that in cases of delay in labour without obvious cause, despite the possibility of a short cord, Caesarean section is not justified before trying the effects of a pitocin drip. If the progress of labour improves but signs of foetal distress appear X-rays should be taken to exclude foetal abnormality, and if none is shown Caesarean section may be justified. If dystocia only becomes apparent in the expulsive stage action must be swift, and forceps should be applied without delay. Blood-stained discharge is not a constant symptom and it may occur before engagement of the head or even rupture of the membranes, and it may justify Caesarean section.

*D. Maxwell*

**94. Prolapse of the Umbilical Cord.**

By P. F. M. Du Toit. *S. Afr. med. J.*, **30**, 1181–1185. Dec. 8, 1956. 9 tables. 2 refs.

The author has reviewed 203 cases of prolapse of the umbilical cord which occurred among 22,923 deliveries in the obstetrical hospitals under the aegis of the University of Cape Town. The present review covers a 3-year period (1st July, 1953 to 30th June, 1956). He has compared this with a previous review in the same institutions (covering a 5½-year period), which was published by Joubert. The incidence in the second series was 1 in 109 cases, whereas in the first series it was 1 in 179. The uncorrected foetal mortality was reduced from 60 per cent in the first series to 45 per cent in the second. Of all the stillbirths in the second series, 10 per cent were associated with prolapse of the cord. In cases in which the foetal heart was heard on admission, 76 per cent survived in the second series as compared with 61 per cent in the first. The foetal mortality was twice as high in non-booked cases as in the booked cases.

With regard to aetiology, it is understandable that if the lower uterine segment and cervix are not well applied to the presenting part, a toneless organ within the

amniotic sac may drop out by force of gravity, or may be washed out by the flow of the liquor. This explains the higher incidence in multiparity, malpresentations, disproportion, prematurity and multiple pregnancy. Low implantation of the cord in placenta praevia may be a cause, as may internal manipulations. It occurred only twice in 847 "surgical" inductions. No cause was found in 30 per cent of cases.

Prognosis depends on the presentation, cervical dilatation and the maturity and condition of the foetus. With breech presentations 60 per cent of infants were born alive as compared with 47 per cent in cephalic presentations, 40 per cent in transverse lie and only 11 per cent in compound presentations. Complete cervical dilatation was associated with a better prognosis in both series, and the results with incomplete dilatation were improved in the second series. The premature infant has less chance of survival.

If the foetus is not alive, delivery should be effected with the minimum of harm to the mother. Marked disproportion and a tightly contracted uterus with a transverse lie should be treated by Caesarean section. In cases in which the foetal heart was heard and cervical dilatation was incomplete, Caesarean section was performed on 69 occasions and 63 live infants were delivered. In 79 similar cases treated conservatively or by version, only 31 survived. Caesarean section was employed much more frequently in these cases in the second series, with a resulting dramatic improvement in foetal salvage. With complete cervical dilatation, Caesarean section is rarely indicated. Delivery should be expedited by vigorous bearing down, episiotomy, forceps, breech extraction or, in cases of transverse lie, by internal version and breech extraction.

*L. J. Abramowitz*

95. **The Fate of the Placenta Left In Situ Following the Delivery of a Fetus in Abdominal Pregnancy.**

By R. S. MILLEN. *Amer. J. Obstet. Gynec.*, **71**, 1348–1352. June 1956. 1 fig. 12 refs.

A case is described of a secondary intra-abdominal pregnancy in which the placenta was adherent in the right upper quadrant of the abdomen, and was left *in situ* when the foetus was removed at laparotomy. The patient had an uneventful recovery but 22 months later developed partial intestinal obstruction. At operation a small yellowish-white mass measuring $5 \times 5 \times 4$ cm. was found attached to the anterior abdominal wall in the right lower quadrant and to several loops of small intestine. This was easily removed and microscopic examination showed it to be placenta with degenerating villi.

[This case shows that sequestration of the placenta is not always devoid of undesirable sequelae. Nevertheless, there is no doubt that it is the best way of dealing with the placenta in nearly all cases of abdominal pregnancy. The author quotes Farris (*Amer. J. Obstet. Gynec.*, 1954, **68**, 1598) as listing only 2 cases that caused trouble later out of 39 abdominal pregnancies in which the placenta was left in the abdomen.]

*F. J. Browne*

96. **The Value of Prophylactic External Version in Cases of Breech Presentation.**

By A. BROSSET. *Acta obstet. gynec. scand.*, **35**, 555–562. 1956. 3 tables. 32 refs.

Writing from a Stockholm Hospital the author divided 147 patients in whom breech presentation was diagnosed and confirmed radiologically into 2 groups: (1) Cases in which external cephalic version was attempted and which were followed up by radiography immediately and then at fortnightly intervals. (Where the procedure was unsuccessful or if the foetus reverted spontaneously to breech presentation, version was again tried at the next follow-up examination.) (2) Cases in which external version was not attempted; these patients, too, were followed up by radiography at fortnightly intervals until delivery.

Prophylactic external version was successful in not more than 30 per cent in the treated group (anaesthesia was not employed), but spontaneous version occurred in 50 per cent of the remaining cases of this group. Thus vertex delivery occurred in 59 and breech delivery in 15 cases. The corresponding numbers in the untreated group were 57 and 16 respectively.

It is concluded that prophylactic external cephalic version is of little value.

[These findings are similar to those obtained by A. J. White, *J. Obstet. Gynaec. Brit. Emp.*, 1956, **63**, 706.]

*N. Alders*

97. **Transvaginal Pudendal-Nerve Block: An Improved Anatomic Approach.**

By P. L. WILDS. *Obstet. Gynec.*, **8**, 385–392. Oct. 1956. 5 figs. 1 table. 4 refs.

**Transvaginal Pudendal-Nerve Block—The Safe Anesthesia in Obstetrics: Report of Seven Years' Experience.**

By J. H. DUGGER, E. E. KEGEL and J. J. BUCKLEY. *Obstet. Gynec.*, **8**, 393–395. Oct. 1956. 3 refs.

The first of these reports comes from the Louisiana State University School of Medicine, New Orleans, and the second from the Episcopal Hospital, Philadelphia. Each is enthusiastic concerning the use of local anaesthesia to block the internal pudendal nerve, the solution being introduced by passing a 20-gauge spinal syringe needle through the vaginal mucosa and sacrospinous ligament just inferior and posterior to the ischial spine on each side. Ten ml. of solution is injected into each side, Xylocaine 1 per cent being as satisfactory as any. So long as care is taken to see that the solution does not enter a vein, the method is free of complications and is very useful in the second stage of labour or for the repair of perineal lacerations. The method is simple and effective.

*J. G. Dumoulin*

## INFANT

98. **Survival of Premature Infants. Classification According to Respiration Rate and Need for Oxygen Therapy.**

By H. C. MILLER. *Obstet. Gynec.*, **8**, 459–464. Oct. 1956. 4 tables. 6 refs.

While the correlation between birth weight of premature infants and survival is good, birth weight is no help in determining which infants of the same weight will live. The trend of the respiratory rate following birth is shown by the author to be a better index of survival than the birth weight.

The material for this study includes 159 consecutively born premature infants, of whom 13 died. No morbidity or mortality occurred among 102 of the infants whose respiratory rates were high or normal during the first hour and subsequently showed no increase. A high morbidity rate and a 25 per cent mortality rate were observed among 52 infants whose respiratory rates increased after the first hour.

The trend of the respiratory rate was of help in judging oxygen needs of the infants.

*J. G. Dumoulin*

**99. A Study of "Post-maturity" in 5,000 Cases.**

By T. F. CORKILL. *N.Z. med. J.*, **55**, 178–183. June 1956. 4 refs.

The study is based on 5,000 personal cases, confined between 1943 and 1954, in which the dates were regarded as reasonably reliable. Sixty-eight cases were rejected because the dates were indefinite. All obstetric deaths were related to the week of delivery. The deaths were tabulated as premature, toxaemia, erythroblastosis, etc., the residue of cases with no clinical abnormality or post-mortem change except asphyxia being described as "unexplained".

The obstetric death rate was lowest in the 40th and 41st weeks, being 14·0 per 1,000, while in the 42nd and subsequent weeks it was 25·4 per 1,000. Of the "unexplained" deaths, the incidence was 8·5 per 1,000 in the 42nd and subsequent weeks, while it was 4·8 per 1,000 for the other gestational periods. Adding deaths due to placental separation, the combined death rate for post-maturity is 11·5 per 1,000. Difficult labour was not a serious contributory factor, only 4 cases occurring in the 1,300 deliveries of the 42nd and subsequent weeks.

The writer suggests that the maximum increased salvage that would be obtained by induction at the 41st week, would be 11·5 per 1,000. To attain this the risks of induction might be 10 per 1,000 or more. He concludes that routine induction at the end of the 41st week is not justified. He considers that induction should be considered in individual cases at the end of the 42nd week, when there are fewer cases, and the foetal risk is greater.

*L. Woodrow Cox*

**100. Postmaturity and the Placental Dysfunction Syndrome.**

By R. H. KUNSTADTER and S. E. SCHNITZ. *J. Amer. med. Ass.*, **161**, 1551–1555. Aug. 18, 1956. 19 refs.

The significance of postmaturity is a matter of controversy. A clinical postmature syndrome has been described by various investigators, and there is a general impression that mortality is higher among postmature infants. The authors consider that the term postmaturity syndrome should be discarded because the signs of so-called postmaturity are really those of inadequate placental function. The clinical signs in the infant characteristic of placental dysfunction are dry, scaling, parchment-like skin; staining of the skin and vernix caseosa; subcutaneous tissue wasting, with evidence of recent weight loss.

In this study 2,877 deliveries were investigated. Postmaturity (defined as a gestational age of 294 days or more) occurred 247 times, and these infants were compared with 252 infants born after the 259th and before the 295th day. The postmature group did not differ significantly as to average weight and body length from the control group, but the placental dysfunction syndrome showing one or more of the signs described did, however, occur in 11 postmature infants. In the full-term group there was only one infant showing these signs. It is evident from this study that the placental dysfunction syndrome, although not confined exclusively to postmature infants, occurs more frequently in this group.

*D. W. James*

**101. A Survey of Cerebral Palsy in Otago.**

By J. BARCLAY. *N.Z. med. J.*, **55**, 199–219. June 1956. 7 tables. 1 fig. 57 refs.

A survey of all known cases of cerebral palsy in Otago, discovered 160 cases. This gives an incidence of 2·5 children born per annum per 100,000 total population. The age, sex, incidence, types of palsy, child rank, incidence of first births, maternal age, incidence of abnormal deliveries, mode of delivery, and treatment, are tabulated. Of the clinical types, 68 per cent were spastic, 4·9 per cent flaccid, 11·8 per cent athetotic, 0·7 per cent rigid, 0·7 per cent had tremor, 2·8 per cent ataxic, 11·8 per cent mixed. Contracture deformities were present in 58·3 per cent.

There was a history of neonatal abnormality in 70·3 per cent of cases, and the incidence of neonatal asphyxia was significantly increased in relation to normal delivery, but not in relation to first births, prematurity and complications of pregnancy. The significance of this group was not established by investigating a group of controls.

There was an incidence of 46·2 per cent abnormal deliveries, including breech 6·7 per cent, forceps 25 per cent, and Caesarean section 7·8 per cent.

*L. Woodrow Cox*

**102. Fetal Poliomyelitis.**

By G. B. ELLIOTT and J. E. MCALLISTER. *Amer. J. Obstet. Gynec.*, **72**, 896–902. Oct. 1956. 2 figs. 16 refs.

The authors report a case of what seems to be undoubted congenital foetal poliomyelitis. The patient acquired the disease at approximately the 8th month of pregnancy and 3 weeks later gave birth to a live infant weighing 4 pounds 3 ounces with "rag doll" flaccidity which lived half an hour. The foetal central nervous system showed well marked changes characteristic of poliomyelitis.

*F. J. Browne*

103. **Pulmonary Hyaline Membrane Syndrome: Some Effects of Oxygen and Amniotic Fluid in its Pathogenesis.**
By L. E. Laufe and S. S. Stevenson. *Obstet. Gynec.*, **8**, 451–458. Oct. 19, 1956. 1 table. 2 figs. 12 refs.

In 1954, the authors reproduced the hyaline membrane syndrome in the lungs of guinea pigs by injecting into their tracheas equal parts of amniotic fluid and plasma. This work suggested that the aspiration of amniotic fluid and pulmonary exudation were intimately associated in the pathogenesis of this disease. Injection of amniotic fluid alone produced extensive atelectasis and vascular congestion. The development of pulmonary exudate, which appears to be necessary for the syndrome, may result from various factors, one of which may be exposure to high-oxygen environment. In these further experiments on guinea-pigs, the authors test this theory and confirm it. Exposure to high-oxygen environment alone does not produce hyaline membrane: if preceded by injection of amniotic fluid into the trachea, it does.

It seems that amniotic fluid can act as a pulmonary irritant and produce an effusion, and by its thromboplastic activity aid in converting fibrinogen into fibrin. Perhaps aspiration of amniotic fluid is the initial pulmonary insult and exposure to a moderately high-oxygen environment perpetuates formation of effusion.

*J. G. Dumoulin*

104. **Adrenals in Anencephaly and Hydrocephaly.**
By K. Benirschke. *Obstet. Gynec.*, **8**, 412–425. Oct. 1956. 1 table. 1 fig. 1 col. plate. 41 refs.

The enlargement of the foetal adrenal glands is due to the presence of a distinct "foetal" zone of the cortex which degenerates for the most part after birth and which comprises approximately 80 per cent of the cortex. In anencephalic monsters, the glands are usually very small and occasionally absent.

Twenty-four cases of anencephaly and 8 cases of hydrocephaly and other cerebral malformation are presented by the author with microscopic findings on the adrenal glands. This study shows that the atrophy of the adrenal glands in anencephaly is due to the premature involution of the foetal zone of the adrenal cortex. Before the twentieth week of gestation this zone is present in its normal development in anencephaly. After this critical period the foetal zone atrophies. In some cases of hydrocephaly the same thing happens.

These findings support the view that the foetal zone of the adrenal gland is governed in the early stages of gestation by chorionic gonadotrophin. Atrophy after the decline in chorionic gonadotrophin secretion by the placenta is thought to be the result of failure of foetal luteinizing hormone production due to a defective hypothalamus. Reduced foetal ACTH production in anencephaly may be an additional factor responsible for the adrenal atrophy in these malformed infants.

*J. G. Dumoulin*

105. **Classification and Causes of Perinatal Mortality.**
By J. P. Bound, N. R. Butler and W. G. Spector. *Brit. med. J.*, **2**, 1191–1196. Nov. 24, 1956.

This paper presents a pathological classification of stillbirths and first-week neonatal deaths based on 337 consecutive necropsies performed at University College Hospital, London. The total number of births during that period was 10,028. In addition, a further 69 neonatal deaths in babies admitted to the U.C.H. Premature Baby Unit from outside sources are included.

The largest group (18 per cent) comprised ante-partum deaths with maceration but without evidence of asphyxia or other pathology. The foetus and particularly the placenta were often smaller than expected.

Among the clinical associations in this group, toxaemia and hypertension occurred in 44 per cent, ante-partum haemorrhage in 15 per cent, multiple pregnancy in 11 per cent and diabetes in 6·6 per cent. Thirty per cent of the mothers were over 35 years old.

Ante-partum asphyxia, often with early maceration, occurred in 10·7 per cent of necropsies. Tardieu's spots were present in 83 per cent of this group.

The clinical associations were identical in this group with those found in ante-partum deaths without evidence of asphyxia. Severe ante-partum haemorrhage, however, occurred in much higher proportion (50 per cent).

Death from intra-partum asphyxia occurred in 16·3 per cent of cases. Thirty-three per cent of these babies were premature; 27 per cent were postmature. Labour lasted over 24 hours prior to foetal death in 38 per cent.

Death from birth trauma occurred in 11 per cent. This was most commonly a tear in the tentorium cerebelli. The clinical associations were most frequently high maternal age, a long labour, traumatic vaginal delivery and multiple pregnancy.

Pulmonary syndrome of the newborn was the final diagnosis in 10 per cent of necropsies. The authors define it as a condition associated with neonatal deaths in the first week of life, characterized by resorption atelectasis together with one or more of the following:

(1) Hyaline membrane, (2) intra-alveolar haemorrhage, (3) pulmonary oedema. Eighty-three per cent of babies with the pulmonary syndrome were premature. The incidence of Caesarean section was increased.

Pneumonia was the cause of death in 5·6 per cent. One-half died within 24 hours of birth and probably acquired their infection before or during labour.

The majority of cases showed foetal distress during labour. There was an increased incidence of Caesarean section and of complicated vaginal delivery and over half were premature.

Intraventricular haemorrhage occurred in 3·3 per cent; all but one were premature. Haemolytic disease caused 4·4 per cent of deaths; congenital abnormalities caused 15·5 per cent of deaths. Hydrocephalus and meningocele were the commonest malformations.

The authors discuss the importance of necropsy in all perinatal deaths and stress the desirability of uniform classification.

*Eileen Wilson*

106. **Classification and Causes of Perinatal Mortality. Parts II and III.**
By J. P. Bound, N. R. Butler and W. G. Spector. *Brit. med. J.*, **2**, 1260–1265. Dec. 1, 1956. 10 tables. 24 refs.

*Part II. Factors in Pregnancy and Labour Influencing Perinatal Mortality*

The authors discuss the clinical associations of major causes of perinatal mortality in 337 consecutive necropsies at the University College Hospital Medical School, London. There was some increase in the perinatal mortality rate when the mother was over 30 years, and a sharp rise over the age of 35 years, both in primiparae and multiparae. This was statistically significant in deaths associated with maceration only, with ante-partum asphyxia and with birth trauma. Toxaemia and hypertension did not entirely account for this increase, although its incidence was significantly raised in the deaths associated with maceration only and ante-partum asphyxia. Prematurity apart, the risk of toxaemia and hypertension in the life of the baby appeared to operate only in the ante-partum period.

The incidence of ante-partum haemorrhage was significantly raised in the maceration and ante-partum asphyxia groups and apparently raised in the pulmonary syndrome group. Postmaturity causes an increased liability to intra-partum asphyxia. This was especially marked when labour lasted over 24 hours. Postmaturity apart, a long labour increased the incidence of death from intra-partum asphyxia, and was more often associated with birth trauma. In assessing the influence of complicated vaginal delivery on the perinatal mortality, the authors differentiate between those manœuvres likely to cause trauma, and those likely to cause interference with the oxygen supply.

The increased incidence of Caesarean section was statistically significant in the pulmonary syndrome and "full-time" pneumonia groups and of borderline significance in the intraventricular haemorrhage group. The pneumonia group was characterized by three features: (1) the association with Caesarean section was confined to full-time babies, (2) the operation was performed for foetal distress, (3) the membranes were already ruptured. In 8 premature babies, however, dying from pulmonary syndrome after Caesarean section, the operation was performed before the onset of labour.

The incidence of multiple pregnancy was raised in all ante-partum deaths, in "full-time" intra-partum asphyxia and birth trauma. The foetal loss among 29 diabetics in the 10,028 deliveries was 24 per cent, all being stillbirths.

*Part III. Clinical Pictures in Babies Dying in the Neonatal Period*

The authors studied 221 neonatal deaths and attempted to correlate clinical and post-mortem findings, and the differential diagnosis. Twenty-seven per cent were due to the pulmonary syndrome, 18 per cent to birth trauma, 15 per cent to congenital malformation, 12 per cent to pneumonia, and 10 per cent to intraventricular haemorrhage. Excluding congenital malformations, the clinical picture of the four groups was often similar and associated with poor conditions at birth, respiratory difficulty and cerebral irritation. In only 24 per cent of foetal cases of cerebral irritation was intracranial trauma found, while in 63 per cent the only abnormal findings were in the lungs.

The pulmonary syndrome was the cause of death in 43 per cent of babies weighing between 1,000 and 2,000 g. at birth. It caused 45 per cent of neonatal deaths following Caesarean section. Only 3 out of the 53 premature infants dying from the pulmonary syndrome first developed symptoms after 12 hours of age. Intraventricular haemorrhage was confined almost entirely to infants weighing less than 2,000 g. at birth. It was found to be impossible to distinguish clinically between intraventricular haemorrhage and the pulmonary syndrome.

Pneumonia was seen most often in pre-viable and in full-time babies. Maternal infection, premature rupture of the membranes, foetal distress or poor condition at birth were very often present and should probably be indications for the administration of prophylactic antibiotics to the baby. Among deaths from intracranial birth trauma, the majority of full-time babies died almost at once, whereas many of the premature babies survived over an hour, and then developed cerebral irritation and respiratory distress. While the differential diagnosis between these groups is often impossible, the authors stress the importance of detecting oesophageal atresia, diaphragmatic hernia and foetal haemorrhage from placental incision during Caesarean section, when treatment may be life-saving. *Eileen Wilson*

## MATERNAL MORTALITY

107. **Experimental Amniotic Fluid Infusion: A Preliminary Report.**

By R. M. Hunter, J. C. Scott, J. P. Schneider and J. A. Krieger. *Amer. J. Obstet. Gynec.*, **72**, 75–78. July 1956. 3 tables. 10 refs.

Because of doubts that have been expressed in many quarters as to the role of so-called amniotic embolism in the causation of sudden maternal death in labour, and more particularly because of the view expressed by Reid, Weiner and Roby (*Amer. J. Obstet. Gynec.*, 1953, **66**, 465) that afibrinogenaemia and intractable post-partum haemorrhage might be due to amniotic fluid infusion, the authors carried out experiments on 2 pregnant bitches at term. Liquor amnii was withdrawn by a hypodermic needle after laparotomy and injected very slowly into a vein. In the first experiment 65 ml. of clear liquor, and in the second 170 ml. of meconium stained liquor was injected. The coagulation time was not changed in either and there was not any abnormal bleeding either from the abdominal wound or from the vagina.

It is concluded that in the pregnant bitch at least amniotic fluid autoinfusion is not a cause either of sudden death or of a fibrinogenaemia.

*F. J. Browne*

## OBSTETRIC OPERATIONS

108. **Controlled Respiration During Cesarean Section.**

By W. K. Bannister. *J. Amer. med. Ass.*, **162**, 1028–1030. Nov. 10, 1956. 5 refs.

The place of general anaesthesia in obstetrics, as opposed to regional methods, has long been a subject of

debate. From the Department of Anesthesiology, Hartford Hospital, Connecticut, the author studied the condition and behaviour of 418 babies born after delivery by Caesarean section. Groups of patients were selected so that causes of depression other than anaesthesia were eliminated, and the cases were divided into three groups according to the type of anaesthetic. Group 1 consisted of 96 mothers who received spinal anaesthesia; Group 2, of 165 mothers who received general anaesthesia (thiopental sodium, cyclopropane with oxygen, and sufficient dimethyl tubocurarine to maintain a quiet operative field); Group 3, of 157 mothers who received similar general anaesthesia but with enough of either dimethyl tubocurarine or succinylcholine to allow complete manual control of the mother's respiration.

The incidence and severity of depression in the babies was least when spinal anaesthesia was given. Comparison of groups 2 and 3 showed that manual control of the maternal respiration resulted in much less depression in the infants of Group 3 than was seen in the infants of Group 2 who were dependent on spontaneous maternal respiration.

*D. W. James*

109. **New Obstetric Forceps with a Split-Universal-Joint Principle.**

By A. Miseo. *Obstet. Gynec.*, **8**, 487–493. Oct. 1956. 6 figs. 2 refs.

The author presents a new and somewhat complicated type of obstetric forceps which embodies the principle of the split universal joint in combination with one adjustable or hinged blade (comparable to the anterior blade of the Barton forceps).

The split universal joint is of the ball-and-socket variety. It is so designed that the hemispheres at the heel of the blades, when locked together, form a complete ball which can be rotated in any plane. Either the blades, which can be completely disarticulated from the handles for cleaning purposes, or the shanks and handles of the instrument can move independently in any direction or angle.

*J. G. Dumoulin*

## GYNAECOLOGY

110. **Ovarian Cervical Stromal Hyperplasia.**

By G. T. Schneider and M. Bechtel. *Obstet. Gynec.*, **8**, 713–719. Dec. 1956. 1 table. 3 figs. 11 refs.

Only in recent years has hyperplasia of the ovarian stroma been recognized as a clinicopathological entity. This condition, found sometimes in the senile ovary, is thought to be a response to hypophyseal stimulation. In it the ovarian cortex is wider and denser than normal, and may assume the shape of spherical masses or whorls. The nuclei of the stromal cells are enlarged. Instead of the small, spindle type of cell, large pale-staining cells resembling lutein cells are seen.

Attention has recently been drawn to a relationship between this condition and endometrial carcinoma. The authors compared the ovaries of 44 patients with such carcinoma with an equal number of controls. Ovarian stromal hyperplasia was noted in 52·3 per cent as contrasted with 35 per cent of the controls.

A similar association has been found between ovarian stromal hyperplasia and ovarian neoplasms such as theca cell tumours and hilus cell (Leydig cell) tumours.

It is possible that a relationship also exists between stromal hyperplasia and mammary carcinoma, and that the rate of growth of metastatic mammary cancer is influenced by hormonal output from hyperplastic ovarian stromal tissue.

*J. G. Dumoulin*

111. **Epilepsy and Menstruation. The Role of Water Retention.**

By B. Ansell and E. Clarke. *Lancet*, **2**, 1232–1235. Dec. 15, 1956. 3 tables. 3 figs. 49 refs.

It has long been suspected that a direct relationship exists between epileptic seizures and menstruation. The authors' investigations of 42 females over a period of 2–4 months support this contention. Sixty-three per cent of the patients reported more fits during menstruation or during the 24 hours immediately preceding it. No correlation between pre-menstrual symptoms and the incidence of fits was found. Pre-menstrual oedema as measured by body-weight changes did not appear to play a primary role in the pathogenesis of menstrual epilepsy, nor did the alteration of sodium metabolism as shown by studies using radioactive $Na^{22}$. All the epileptics investigated had a normal total body-water, and those with and those without a menstrual aggravation of the seizures showed no difference. The authors conclude that it seems possible that the complex hormonal changes that take place may play a prominent part.

*H. H. Fouracre Barns*

112. **Catamenial Epilepsy.**

By J. Laidlaw. *Lancet*, **2**, 1235–1237. Dec. 15, 1956. 1 table. 1 fig. 8 refs.

The author records his observations on the relationship between seizures and menstruation in 50 epileptic in-patients. An increased incidence of fits immediately before, during and after menstruation was observed, 72 per cent of the patients showing clear evidence of the relationship. In addition a definite mid-luteal reduction in fits occurred. The author suggests that a protective influence operates during the luteal phase and that this may be due to an anticonvulsant action of progesterone.

*H. H. Fouracre Barns*

113. **Suppression of Ovulation by Tri-*P*-Anisyl Chloroethylene (TACE).**

By R. W. Kistner, C. J. Duncan, Jr., and H. Mansell. *Obstet. Gynec.*, **8**, 399–407. Oct. 1956. 3 tables. 4 figs. 11 refs.

TACE is a synthetic pro-oestrogen claimed to have a prolonged effect, probably as a result of fat storage. It was used in 44 cases by the authors to inhibit ovulation, in 24 because of symptomatic endometriosis, 13 because of primary dysmenorrhoea and 7 because of pre-menstrual tension. A twice daily dose of 24 mg. given orally was found to inhibit ovulation and was used for

up to 100 days. TACE does not produce significant nausea or vomiting but may cause endometrial hyperplasia with profuse breakthrough bleeding or severe withdrawal flow. Smaller dosage (24 mg. daily) will produce anovulation without breakthrough bleeding or excessive hyperplasia.

The treatment produced symptomatic improvement in all cases both during and after the therapy.

*J. G. Dumoulin*

**114. The Unknown Abortion as a Cause of Apparent Primary Sterility in Women.**

By E. MARIN BONACHERA and J. BOTELLA-LLUISA. *Ann. Ostet. Ginec.*, **78**, 34–42. 1956. 6 figs. 13 refs.

The material on which this paper is based is taken from a survey of 1,000 endometrial biopsies from cases of primary sterility. The biopsy was performed before or during the menstrual period. In 24 out of the 1,000 cases, abortion rests of varying ages were found. It is suggested that these unsuspected abortions, which were found in 2·4 per cent of women with primary sterility may take place before the first missed period. It was also noted that the tubes were closed in a substantial proportion of these cases.

*Josephine Barnes*

**115. The Use of Isotopes ($Au^{198}$) in the Study of Isoperistaltic Tubal Permeability.** (Emploi des radio-isotopes ($Au^{198}$) pour l'étude de la perméabilité tubaire isopéristaltique.)

By A. STABILE and F. LEBARGNE. *Gynéc. prat.*, **7**, 259–267. 1956. 1 fig. 6 refs.

The authors present a preliminary report on a new method for the investigation of tubal permeability. They feel that the conventional methods only demonstrate the physical patency of the tube and not its ability to transport an ovum from the ovary to the uterus. Various workers have endeavoured to recover from the cervical mucus dyestuffs and colloidal materials injected into the peritoneal cavity, but the difficulty has been in the accurate and easy recovery of the substances used, from the cervical mucus. The authors claim to have overcome this difficulty by the use of radioactive gold. At about the expected time of ovulation, 25 to 50 microcuries of $Au^{198}$ are injected into the peritoneal cavity at about the midpoint of a line from the umbilicus to the anterior superior iliac spine.

A vaginal tampon is inserted and changed each day for the next four days. When removed, each tampon is scanned by a Geiger counter or a scintillation counter. The presence of radioactivity indicates tubal patency.

Although no figures are given, the authors claim that the total amount of radioactivity to which the pelvic organs are exposed is rather less than that given by a single X-ray of the pelvis. They also claim that the gold is in no way absorbed.

At the moment the method should be regarded as experimental and though the authors feel that a positive result is reliable, a negative one should be checked by the more usual methods of tubal investigation. They have found cases in which tubal patency was demonstrated by hysterosalpingography although the $Au^{198}$ test had been negative. They suggest this apparent contradiction may be due, not to errors of technique, but to the physiological inability of the tube to transport the injected material in the direction in which it would have to transport an ovum.

*Geoffrey Dixon*

**116. The Post-Coital Test.**

By G. I. M. SWYER. *Ann. Ostet. Ginec.*, **78**, 43–55. 1956. 5 figs. 8 refs. [In English.]

This is an account of 638 post-coital tests performed in 394 women complaining of infertility. Two hundred and ten were made on women who subsequently conceived and 428 on 354 patients who have failed to conceive.

The quality of the cervical mucus was found to be little different in those who did and did not conceive, though sperm invasion was better in those who conceived. The period of abstinence preceding coitus has little influence on the ultimate result. The time between coitus and examination of the cervical mucus is also unimportant and up to 18 hours may elapse without vitiating the result.

The day of the cycle on which the test is performed is important. The most acceptable results were obtained between the 11th and the 14th day of the cycle, or 13 to 18 days before the next expected menstrual period. The differences at different times in the cycle are most marked in relation to the quality of the cervical mucus, and less in relation to sperm invasion and activity.

With adequate seminal fluid, the chance of a positive post-coital test was greater when the mucus was acceptable than when it was not. Positive post-coital tests were obtained when the semen was of poor quality, so that a post-coital test should always be performed before giving an unfavourable opinion regarding the husband's fertility.

The post-coital test is an essential part of the investigation of infertility and may bring to light many factors, including mechanically inadequate coitus, which appears to be frequent in cases of infertility.

*Josephine Barnes*

**117. Hypopituitarism and Gonadal Dysgenesis. The Relation of the Pituitary Gland to Sexual Differentiation.**

By W. P. U. JACKSON and R. HOFFENBERG. *Lancet*, **2**, 1237–1239. Dec. 15, 1956. 2 figs. 9 refs.

A case of congenital hypopituitarism associated with hypogonadism and hypothyroidism is reported. The patient exhibited mild male pseudohermaphroditism. The authors suggest that the hypopituitarism led to secondary partial gonadal failure.

*H. H. Fouracre Barns*

**118. Urethro-Vaginal and Vesico-Vaginal Fistulae. A Summary of 57 Cases Encountered in the Groote Schuur Hospital, Cape Town, January 1952 to July 1956.**

By J. T. LOUW. *S. Afr. med. J.*, **30**, 1103–1108. Nov. 17, 1956. 2 tables. 9 figs. 7 refs.

The author discusses the aetiology, symptoms and

signs, treatment, and the results obtained in 57 cases of urethro-vaginal and vesico-vaginal fistulae.

The better the medical services in a community, the lower the incidence of fistula. The high incidence in the rural Bantu with a witch-doctor mentality can be easily understood. Of the 57 cases, 41 followed labour, 12 followed operative procedures and 4 were caused by inflammation. All the Bantu cases followed parturition, whereas only 2 of the 7 cases in Whites followed labour. In the Coloured people an intermediate figure was found.

Sloughing and trauma are the main causes of fistula. The former may be due to continuous and excessive stretching of the base of the bladder, thus interfering with the blood supply, or it may be due to pressure of the presenting part for an abnormally long time. It may also occur post-operatively if a small portion of the bladder wall becomes strangulated in a suture when the vaginal vault is being stitched. Interference with blood supply may occur with radical pelvic surgery. There were no such cases in 97 Wertheim operations, and it occurred as a complication in 2 of 12 cases of posterior exenteration. Abscess formation, primarily in urethral diverticuli, was the cause in 2 cases. In 1 case abscess formation following hysterectomy produced a fistula. No patients with neoplastic infiltration are included, and there were no cases of irradiation fistulae.

Trauma may be caused by instruments, spicules of foetal bone, rarely during difficult pelvic operations and very occasionally by an accident. Intercourse is a major problem in the post-operative period.

Symptoms and signs are usually painfully obvious. A good history, a 3-swab test and examination under anaesthesia aided by injection of dye into the bladder will serve to make a positive diagnosis.

With regard to treatment, more team work between medical and nursing staffs is required than in most other surgical problems. Pre-operatively syphilis and deficiency states must be treated. Oestrogens are administered in post-menopausal patients, and the urine must be rendered sterile and acid, the latter to dissolve crusts. In large fistulae ureteral orifices must be located.

At operation two main principles must be observed, viz., the raw edges must be opposed and interference with wound healing must be prevented. This is easy in small mobile fistulae, with counter-incisions to relieve tension. Difficulty arises with large, hard fixed fistulae. Methods of mobilizing and utilizing the cervix and uterus, and of using the labia as a pedicle graft are described. Other methods employed by Ingelman-Sundberg and Bastiaanse are discussed. Ureteric transplantation was not performed, but in 2 cases ileal bladders were constructed. A method of urethroplasty is described. At no time were special instruments or sutures used.

In all cases a suitable catheter is stitched into the urethra post-operatively and it is connected to a low-pressure suction apparatus after blood clots have been washed out of the bladder.

Antibiotics are administered and bladder distension is avoided. The catheter is washed out 8-hourly and it is removed on the 12th day. Patients are made to void urine at regular definite intervals. They are strongly advised to avoid intercourse for 3 months and to inform their doctor that they have had a fistula should they become pregnant.

Treatment was successful in 50 of the 57 cases. Details of the 7 patients in whom it failed are discussed.

*L. J. Abramowitz*

**119. *Hemophilus Vaginalis* as an Etiological Agent in Vaginitis.**

By J. L. RAY and G. M. MAUGHAN. *West. J. Surg. Obstet. Gynec.*, **64**, 581–587. Nov. 1956. 2 refs. 3 figs.

*Haemophilus vaginalis* is thought to be responsible for the majority of cases of "non-specific" vaginitis. The authors consider it to be distinct from *H. influenzae* and it appears to be of low virulence and is difficult to recover on culture. Two groups of patients were investigated; 447 clinic patients, one-third of whom were pregnant, and 74 private patients with vaginitis with 11 of their husbands. Each patient had 2 Gram stain slides taken, one wet smear and 2 vaginal smears for cancer. Slides were checked for *Trichomonas* and *Candida albicans* and cultures prepared in blood and chocolate agar, trypticase, thioglycolate, ascitic fluid and rabbit blood agar. Of the 447 clinic patients, 154 had infective organisms present, 44 per cent with *H. vaginalis*. Thirty-one patients had both *Trichomonas* and *Haemophilus* and 5 had both *Monilia* and *Haemophilus*. Nineteen of the 68 patients with *Haemophilus* were symptom-free and those patients with symptoms described them as mild. Treatment was carried out with Triple Sulpha cream, Vagisec, Sterisil, Mycostatin, Gentersal and penicillin. No one particular agent proved very effective but when failure occurred the infection would frequently respond to another agent; taken overall the rate of cure was 79 per cent.

*D. C. A. Bevis*

**120. Tritheon in Trichomonas Vaginitis. A Critical Evaluation.**

By H. L. GARDNER and C. D. DUKES. *Obstet. Gynec.*, **8**, 591–596. Nov. 1956. 2 tables. 6 refs.

Forty-four patients were treated by the authors with oral Tritheon for trichomonas vaginitis. One 100 mg. Tritheon tablet was taken 8-hourly by each patient and her husband for 15–30 consecutive days.

The result of the treatment was disappointing in that all patients yielded wet mounts positive for trichomonas within 13 days of completion of treatment, although half the patients showed clinical improvement. In addition, a number of cases showed side-effects which included nausea, anorexia, abdominal cramps, lethargy, swelling of hands and feet, and (in one case) severe erythema multiforme.

*J. G. Dumoulin*

## NEW GROWTHS OF THE REPRODUCTIVE ORGANS

**121. The Diagnosis of Early Genital Cancer and Other Abnormalities by Cytology. A Pilot Survey.**

By N. D. CONSTANTINE and D. MOORE. *S. Afr. med. J.*, **30**, 1201–1209. Dec. 15, 1956. 9 figs. 38 refs.

In the United States 26,000 women die annually as the result of uterine cancer. It is estimated that 60 out of every 100 women present themselves too late for adequate treatment. Early diagnosis and immediate treatment still carry with them the best possible prognosis. Examination of exfoliated material is not a substitute for biopsy or curettage, but should be accepted as a preliminary method in the diagnosis of early cancer. The history of cytological diagnosis is traced from 1853, when Donaldson described cells seen in "tumour juice". Methods of collecting material are described, and the authors favour a combination of the methods of Papanicolaou and Ayre.

For the past 18 months cytological studies have been carried out at a specialized clinic in the Gynaecological Out-Patient Department of the Groote Schuur Hospital, Cape Town. Two thousand one hundred and fifty smears from 1,050 patients were examined. Statistical analysis is to be carried out when adequate follow up of patients' case histories has been completed.

A large number of smears were also examined for oestrogenic dysfunction and chromosomal sexing. *Trichomonas vaginalis* and *monilia* were also well demonstrated. In many cases of trichomoniasis the normal morphological characteristics of the cells were retained. Ayre suggests that this variety of trichomonad is of low irritative type, as distinct from those cases in which cells show inflammatory hyperplasia. The authors believe that trichomonas infestation is considerably more general than commonly believed.

Numerous staining techniques are described. The haematoxylin-and-eosin method has limitations in smears presenting an indeterminate morphology. Fixation of smears is discussed. On no account should the smear be allowed to dry before fixation. The procedure followed, in all essential points, is that advocated by Papanicolaou.

The normal histological features of vaginal cells, cervical cells, endometrial cells and histiocytes are described. It may be very difficult to differentiate ecto-cervical cells from cells shed in the lower vagina. Although rarely present in the normal vaginal smear, histiocytes constitute some of the most difficult cells with which the cytologist has to contend since they are of many types and exhibit marked pleomorphism. The criteria of malignancy are discussed. A positive diagnosis is made by the evaluation of various factors, the most important of these being nuclear changes. There may be variation in nuclear size or shape. One may find giant nuclei, fragmented nuclei or bizarre shapes. The chromatin may be clumped or its distribution changed. Occasionally it presents as a thickened nuclear membrane. Multinucleate cells may be present. Mitotic figures are of relatively little importance. With regard to cytoplasmic changes, abnormal cells are usually large, but the increase in cytoplasm is generally not proportionate to the increase in size of the nucleus. Bizarre forms are commonly seen such as the tadpole cells in squamous carcinoma, and embryonic forms in poorly differentiated types. In adenocarcinoma the cells are generally of the round type, in spindle-cell carcinoma fibre-like, whereas in endometrial carcinoma the shape or form is more regular. Vacuolization is frequently seen.

At Groote Schuur Hospital all patients with cervical erosion are referred to a special clinic. Two smears are taken, 1 from the posterior fornix and 1 by Ayre's method. The cervix is inspected macroscopically and in many cases with the aid of the colposcope. After cleaning with N/10 acetic acid, Schiller's iodine is applied. Areas which do not take up the stain are charted. In the majority of cases the endocervix is cauterized with the "hot-point" electric cautery, and the eroded area is seared in a radial manner. Antibiotic pessaries are prescribed for 10 nights. The patient returns in 6 weeks and if the smear has been positive or doubtful she is admitted for diagnostic curettage and cervical cone biopsy.

Though the statistical analysis of the 1,050 cases is not complete, 1 case of early carcinoma and 4 cases of carcinoma *in situ* are reported as illustrative. Reicher, Massey and Bechtold (*Amer. J. Obstet. Gynec.*, 1950, **59**, 860) who studied 3,500 smears reported a combined error of 0·74 per cent. Cuyler *et al.* (*Amer. J. Obstet. Gynec.*, 1951, **62**, 262) are of the opinion that many cases of intraepithelial carcinoma would be missed unless routine cytological studies were made on women as young as 20 years of age. Pund and Auerbach (*J. Amer. med. Ass.*, 1946, **131**, 960) studied 1,200 surgically removed cervices and found pre-invasive carcinoma in 3·9 per cent.

Theoretically all cases of carcinoma of the cervix would be curable if the diagnosis were made early enough, and early detection is thus the key to the control and cure of cancer. As Papanicolaou has stated, the cytological method is still going through a period of evolution, and that our present achievements do not actually represent our maximum expectations in this new field.

*L. J. Abramowitz*

122. **Diagnosis of Uterine-Tube Carcinoma by Vaginal Cytology.**

By J. I. BREWER and A. M. GUDERIAN. *Obstet. Gynec.*, **8**, 664–672. Dec. 1956. 9 figs. 23 refs.

Positive and atypical vaginal cytosmears were found in 3 patients with carcinoma of the Fallopian tubes. Curettage of the uterus and biopsies of the cervix failed to demonstrate carcinoma of the uterus in 2 of the 3 patients. Curettage was impossible in one case due to cervical stricture.

Persistently positive cytosmears in cases in which diagnostic curettage and cervical biopsies are negative suggest that a neoplasm may be in the tube, ovary or peritoneum.

*J. G. Dumoulin*

123. **Cancer of the Cervix: An Appraisal.**

By J. V. MEIGS. *Amer. J. Obstet. Gynec.*, **72**, 467–478. Sept. 1956. 9 tables. 16 refs.

Selection of cases either for surgery or for radium is the real advance in treatment of cancer of the cervix in

the last 5 years. The combination of full radiation (X-ray and radium) treatment and radical surgery is a mistake, and can have serious consequences.

The author discusses diagnosis in some detail. A vaginal smear should be taken from the pool behind the cervix before any examination by finger or speculum. The speculum should be introduced without bruising the cervix and without a lubricant, and with only water to moisten it. Examination by the colposcope is of value in that many abnormal types of epithelium may be seen and become familiar to the colposcopist, though Meigs has never made the diagnosis of cancer of the cervix because he used the colposcope. The Schiller test is useful using double strength Schiller solution (2 parts of iodine, 4 of potassium iodide and 300 of water). Biopsies are taken from the junction of the stained and unstained areas. The cervical canal is curetted with a sharp curette. If the smear is positive or the biopsy shows cancer *in situ* the patient should be examined under anaesthesia and a cone removed with a sharp knife, not diathermy.

Details are tabulated of 5 and 10 year cures by surgery, radiation and combinations of both, all the operations having been done by the author. Of 61 cases in stages 1 and 2, 55 (90 per cent) were alive and without signs of recurrence after 5 years. All were treated by surgery only. There were 29 cases in stages 1, 2 and 3 treated by surgery following radiation (radiation failures) and of these 18 (62 per cent) were well after 5 years. Of 20 cases in stages 1 and 2 treated by surgery following radiation (no cancer at operation, radiation cures) 19 were well after 5 years (95 per cent). This suggests that radiation cured malignant lymph nodes. The cure rate of patients with positive nodes was excellent, running from 31 to 55 per cent in the 5-year results, and to 25 to 40 per cent in the 10-year results. The study suggests that radiation and surgery are complementary and that results in the hands of experts will be good whatever method is used but it also suggests the importance of selection.

*F. J. Browne*

124. **Cervical Cancer. Factors Influencing Prognosis in Intraepithelial and Clinical Carcinoma of the Cervix Uteri.**

By C. B. Brack, L. Townsend, B. W. Haines and R. J. Dickson. *Obstet. Gynec.*, **8**, 728–735. Dec. 1956. 15 tables. 29 refs.

During the years 1940–1949 702 patients with carcinoma of the cervix were treated at the Johns Hopkins Hospital, 93 having Stage 0 growths. Ninety-seven per cent of the cases have been followed up.

The Stage 0 cases were usually treated by total hysterectomy and bilateral salpingo-oöphorectomy. The Stage 1–4 cases were treated with radium and deep X-ray therapy, only 21 being treated surgically.

The results of treatment for the second 5-year group were better than those for the first 5 years. This was due to a greater percentage of early cases in the total number, and not to improvement in therapy.

The younger the patient, the more advanced was the growth at the time of diagnosis. Thereafter, age did not affect the prognosis. The parity of the patient does not affect the survival rate. The prognosis is not affected by the type of tumour cell despite the fact that spinal cell tumours are theoretically radio-resistant and basal cell tumours highly radio-sensitive.

*J. G. Dumoulin*

125. **Diagnosis of Ovarian Carcinoma by Vaginal Cytology.**

By D. C. Figge and R. R. De Alvarez. *Obstet. Gynec.*, **8**, 655–663. Dec. 1956. 1 table. 5 figs. 10 refs.

Ten patients with ovarian malignancy had smears taken from the vaginal pool and squamo-columnar junction and the smears were evaluated and classified according to Papanicolaou's method. Seven of the smears were diagnosed as malignant and 2 as highly suspicious. Small atypical glandular cells were uniformly exhibited in the vaginal smear of each patient with ovarian carcinoma. The occurrence of positive vaginal smears in such a proportion of ovarian carcinoma studied suggests that serial vaginal smears may offer a potential aid in the early diagnosis of ovarian malignancy when screened by experienced cytologists.

*J. G. Dumoulin*

126. **A Clinical and Pathological Study of Endometriosis of the Lung.**

By R. Lattes, F. Shepard, H. Tovell and R. Wylie. *Surg. Gynec. Obstet.*, **103**, 552–558. Nov. 1956. 8 figs. 20 refs.

This is a report from New York of a case of endometriosis of the lung. It occurred in a 34-year old woman who, for about 3 years, had episodes of haemoptysis associated with the menses. These haemoptyses started following a Caesarean section and an endometrial curettage for menorrhagia, and continued irregularly in spite of various hormonal treatments, until she again became pregnant. At about this time X-ray studies of the chest, which had previously been negative, showed a discrete coin lesion in the right middle lobe. Exploratory thoracotomy followed by segmental resection showed that the pulmonary mass consisted of endometrium with marked decidual reaction of the stroma. It was this decidual reaction which caused the previously present and functioning endometrial implant to enlarge and become detectable on X-ray. The patient has since been delivered at term by Caesarean section and no further haemoptyses have occurred.

After a very brief review of the most popular theories on the pathogenesis of extra-genital endometriosis, it is suggested that none of these theories explains satisfactorily all cases. For the case reported, it is believed that haematogenous transportation and implantation of viable endometrium at the time of the previous uterine operations is the most plausible explanation.

*John P. Erskine*

## OPERATIONS

127. **Culdoscopy. An Extraordinarily Simple and Safe Procedure.** (Pelvioscopie transvaginale. Une technique extraordinairement simple et sure.)

By A. R. Abarbanel. *Gynéc. prat.*, **7**, 269–282. 1956. 5 tables. 4 figs. 5 refs.

The author reviews 500 cases in which culdoscopy was performed. The principal indications were:

(1) Unexplained sterility.
(2) Obscure pelvic lesions and pain.
(3) Oligomenorrhoea and secondary amenorrhoea.
(4) The possibility of an ectopic pregnancy.

In this series he has had 21 unsuccessful attempts, for a variety of reasons, and including 5 in which the intestine was perforated.

In patients investigated for infertility by this means pathological lesions were found in 58·7 per cent of cases of primary infertility and 64·3 per cent of cases of secondary infertility. The author considers culdoscopy a most valuable method of gynaecological diagnosis and lays stress on its safety.

The technique used is described in great detail. Normally the investigation is carried out on the conscious patient but the author suggests that experience can be gained by carrying out culdoscopy before laparotomy.

*Geoffrey Dixon*

128. **Surgical Curettage. Its Value in Abnormal Uterine Bleeding.**

By R. C. Benson and J. N. Miller. *Obstet. Gynec.*, **8**, 523–530. Nov. 1956. 3 tables. 4 figs. 7 refs.

A series of 647 pre-menopausal patients with abnormal uterine bleeding had surgical curettage during the years 1951–1955 at the University of California Medical Center, San Francisco. Excluded from the series were patients over 50 years of age, those with pregnancy complications, visible lesions of the cervix, and cases with cancer-positive vaginal smears. About half the cases had menorrhagia and half metrorrhagia. Eight patients had unsuspected adenocarcinoma of the fundus and 12 occult squamous cell carcinoma of the cervix on curettage, a 3 per cent incidence of malignancy in the series.

The cases were divided into two groups: (1) those with hypermenorrhoea, and (2) those with metrorrhagia. Of the 323 cases in Group 1 92 were treated by hysterectomy or with radium, whereas 37 out of 324 cases in Group 2 were so treated. In Group 1 162 were followed up for 3 months or longer and 48 per cent of them, compared with 65 per cent of 192 in Group 2 were cured by the curettage. Adjunct hormone therapy increased the effectiveness of treatment to 68 and 75 per cent respectively in the two groups. Thus, curettage is of both diagnostic and therapeutic value.

*J. G. Dumoulin*

129. **Surgery for Cervical Carcinoma.**

By C. T. Beecham. *Obstet. Gynec.*, **8**, 482–486. Oct. 1956. 10 tables.

Although irradiation has remained the traditional therapy for carcinoma of the cervix, 103 out of 265 patients treated at Temple University Hospital, Philadelphia, have been subjected to surgery. Thirty-two were given pre-operative irradiation.

The author advocates the Wertheim procedure without lymph node dissection and with conservation of the ovaries in carcinoma *in situ*. Irradiation seems as effective as surgery when the cancer has spread to the lymph nodes. However, residual cancer in the cervical stroma seems to occur in a high percentage of cases. Therefore, the author suggests a semi-radical operation should be performed on the irradiated group 6 months later; resection of lymph nodes adds nothing to the salvage of an irradiated patient but increases the chance of fistula formation.

If it is evident that the cancer is not responding to irradiation full-scale radical surgery, including node dissection, is indicated.

*J. G. Dumoulin*

130. **Surgical Management of Carcinoma of the Cervix.**

By J. W. Kelso. *Surg. Gynec. Obstet.*, **103**, 565–568. Nov. 1956. 5 refs.

This report from Oklahoma summarizes an experience of 10 years in the surgical management of cancer of the cervix. The material consists of 89 patients operated on 5 or more years ago. All cases of carcinoma of the cervix in which there was reasonable hope of surgical extirpation of the disease have been accepted for operation. The operative procedure consisted of radical Wertheim hysterectomy followed by deep X-ray therapy.

Of the 89 cases of proved invasive carcinoma, 60 were Stage I (International Classification) and 29 were Stage II. Of the 60 Stage I cases, 52 patients are alive and free of any evidence of residual disease, making an 86·6 per cent 5-year survival rate; and of the 29 Stage II cases, 20 patients are alive and well, making a 68·9 per cent 5-year survival rate.

In the group of 89 patients, nodal involvement was demonstrated in 15 and of these 9 or 60 per cent are alive and well. Of the 89, 4 were connected with pregnancy and 5 patients had carcinoma in cervical stumps. All are alive and well. Seven patients had columnar cell carcinomas and of these only 3 have survived.

The operative mortality was 2·5 per cent and 5 cases developed fistulae.

The author is convinced that surgery has a place in the treatment of carcinoma of the cervix for 2 reasons:

(1) The salvage rate is as good or better than that for patients treated by other methods.

(2) The psychological effect upon the patient is far more powerful and realistic in those managed by surgery than in the patients treated by radiation.

*John P. Erskine*

131. **Urinary Tract Fistulas Following Radical Surgical Treatment of Carcinoma of the Cervix (Exclusive of Exenterations).**

By A. Brunschwig and H. C. Frick. *Amer. J. Obstet. Gynec.*, **72**, 479–488. Sept. 1956. 8 tables. 1 ref.

During the period September 1947 to December 1950, 212 operations envisaging cure were performed for cancer of the cervix in stages 1, 2, 3 and 4. This number is exclusive of exenterations, but includes instances of recurrent carcinoma following radiation therapy. The type 4 cases in the series had segmental resections of bladder or ureter or ligation of the ureter above transection. The operation usually included a radical

panhysterectomy with pelvic node dissection. In the earlier periods of the series the ureters were completely mobilized from the pelvic brim to the bladder and were rather closely stripped of connective tissue, no attempt being made to preserve arteries, and all tissues in the lateral pelvic spaces including peritoneum, were resected. At present the periureteral connective tissue is preserved and also the mesial leaf of peritoneum attached to the upper half of the pelvic segment of the ureter.

Following the 212 operations there were 50 fistulae (23·5 per cent). Of these 14 were vesico-vaginal and 21 uretero-vaginal. All resulted from ureteral or bladder injury at operation that was repaired and later broke down, or were fistulae that developed after operation, as a result of ischaemia.

Among the 21 uretero-vaginal fistulae 9 resulted from accidental division of the ureter with immediate repair over catheter. All these immediate repairs broke down, probably because the ureter had been trimmed rather closely with a radical excision of pelvic peritoneum and connective tissues. The remaining 12 uretero-vaginal fistulae were due to post-operative ischaemia, the ureters at the time of operation having appeared uninjured. Three of these were bilateral and one developed a month, and another two months after the operation.

The 14 vesico-vaginal fistulae were put on continuous catheter drainage as soon as the diagnosis of fistula was made and 7 of these healed spontaneously.

It is considered that uretero-vaginal fistulae due to ischaemia may be observed for at least 6 months in the hope that spontaneous closure will occur, but few do so —only one in a total of 21 patients in the present series. There was no evidence that pre-operative radiation contributed to ischaemic post-operative fistula formation.

It is hoped that the less radical ureteral stripping now adopted and preservation of its blood supply will reduce the incidence of ureteral fistulae in the future.

*F. J. Browne*

132. **A New Contrast Medium (Salpix) for Hysterosalpingography.**

By A. SHARMAN. *Ann. Ostet. Ginec.*, **78**, 166–171. 1956. 6 figs. 26 refs. [In English.]

A review is given of the use of iodized oils for hysterosalpingography. The undesirable features of these substances lie chiefly in the retention of the oil and its slow rate of absorption. Even in the absence of infection, retention of oil may lead to the formation of pelvic adhesions, and to the setting up of a foreign-body reaction around oil retained in the Fallopian tubes.

The new medium "Salpix" has as its base polyvinylpyrrolidine, a blood substitute, and its iodine containing component is the organic compound acetrizoate. This compound is sufficiently viscous to diagnose permeable tubal strictures within an hour or a little longer. It is rapidly absorbed, has a high iodine content and yet yields little free iodine.

*Josephine Barnes*

133. **Present Status of Plastic Operations on the Fallopian Tubes.**

By J. P. GREENHILL. *Amer. J. Obstet. Gynec.*, **72**, 516–522. Sept. 1956. 45 refs. 1 table.

The author has collected data on 2,113 plastic tubal operations for sterility performed in the U.S. and other countries. The operations were followed by 405 pregnancies but there were only 313 living children (15 per cent) or 1 living child for every 7 operations. Of 286 pregnancies regarding which data were available 45 were in the tube (15·7 per cent) or 1 tubal pregnancy for every 6 operations. While these results are much better than those recorded by him after a similar enquiry in 1937 (36 live babies after 711 salpingostomies) they are far short of what they should be to justify plastic operations except by those who are specially experienced in the technique, especially as results almost as good can be got by non-surgical treatment.

*F. J. Browne*

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Dates should be given as 10th May, 1946, and *not* 10.V.46. Numbers should be in the form of numerals and not words except when beginning a sentence, thus "Fifteen patients out of a total of 60 exhibited," etc. The official rather than the proprietary names of drugs must be used. The Journal convention is gr. for grains; g. for grammes; Kg.; ml. (*not* c.c. or c.cm.); mg.; pounds (*not* lb.); ounces (*not* oz.), etc., and wherever suitable the metric equivalent of an English measure should be given, for example, when recording pelvic measurements, size and weight of babies, tumours, etc.

When comparable figures are given, either the English or the metric mode must be followed, thus: the excretion of urine/24 hours should be shown in ml. (and not ounces) when the urinary or blood-urea is given in g./100 ml.

REFERENCES

In the text the author's name should be given, with the date of publication and the list of authors quoted put at the end of the text in alphabetical order as in the Harvard Scheme: Author's name, initials, year of publication (in brackets), name of journal (*italics* abbreviated), volume number (underlined) and page number. In the case of books the order is: Author's name, initials, year of publication, full title (*italics*), edition, publisher and place of publication, page, thus:

Brown, H. E., and Jones, B. K. (1943): *J. Obstet. Gynaec. Brit. Emp.*, **2**, 128.

Sampson, P. (1940): *Obstetrics for Midwives*. 2nd edition. Fraser, London. p. 9.

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